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Nos. 2-3

CONTENTS.

1 The Pathological Changes in the Neurone in Nervous Disease.
—WILLIAM G. SPILLER, M.D.

2 Pathological Report on a Case of Dermatitis Vesiculo Bullosa et Gangrænosa Mutilans Manuum (Duhring), with a Consideration of the Relations of Vascular and Nervous Changes to Spontaneous Gangrene and Raynaud's Disease.
—DR. WILLIAM G. SPILLER, M.D.

3 Renaut's Bodies in a Case of Vesiculobullous Dermatitis and Gangrene.
—WILLIAM G. SPILLER, M.D. 2 plates to fa
of this artic

4 A Case with the Symptoms of Cerebro-Spinal Meningitis, with intense and Cerebral Alteration of the Nerve Cell Bodies, but with little evidence of Inflammation.
—WILLIAM G. SPILLER, M.D.

5 A Case of Malaria presenting the Symptoms of Disseminated Sclerosis, with Necropsy.
—WILLIAM G. SPILLER, M.D.

6 Cerebellar Lesions without Cerebellar Symptoms . . . WILLIAM G. SPILLER, M.D., W. E. ROBERTSON, M.D., and W. S. WADSWORTH, M.D.

7 Asthenic Bulbar Palsy . . . CHARLES W. BURR, M.D., and D. J. MCCARTHY, M.D.

8 The Rapid Diagnosis of Rabies.
—MAZŸCK P. RAVENEL, M.D., and D. J. MCCARTHY, M.D.

9 Remarks on the Importance of the so-called Specific Lesions of Rabies.
—WILLIAM G. SPILLER, M.D.

10 Acute Internal Hydrocephalus: A Clinical and Pathological Study.
—CHARLES W. BURR, M.D., and D. J. MCCARTHY, M.D. 1 pl. n. m. to face
of this article

11 Observations of Blood Changes Following Celiotomy . . . . . . C. Y. WHITE, M.D.

12 The Blood in Infancy and Childhood . ALFRED STENGEL, M.D., and C. Y. WHITE, M.D.

13 Granular Degeneration of the Erythrocyte.
—C. Y. WHITE, M.D., and WILLIAM PEPPER, M.D. 1 pl. n. m. to f
page 4

14 A Study of Congenital Sarcoma of the Liver and Suprarenal . WILLIAM PEPPER, M.D.

15 The Carbohydrates of the Urine in Diabetes Insipidus . . . DAVID L. EDSALL, M.D.

16 Carcinomatous Degeneration of a Papilloma of the Conjunctiva with Infiltration of the Eyelids . . . . S. D. RISLEY, M.D., and E. A. SHUMWAY, M.D.

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(*b*) THE PATHOLOGICAL CHANGES IN THE NEURONE IN NERVOUS DISEASE.[1]

By William G. Spiller, M.D.,

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In discussing the pathological changes in the neurone in nervous disease the most important question we have to answer is: Does pathology afford any support for the neurone doctrine—*i. e.*, are the changes that occur in disease of the nervous system of such a character that we may obtain from them evidence of the existence of neurones?

To answer this question it must be shown whether degenerative processes have a tendency to affect distinct groups of nerve cells, including their dendritic processes, axones, collaterals and terminal ramifications, to the partial or complete exclusion of other groups.

It must be shown whether the neurone in its entirety, either motor or sensory, is affected by disease—i.e., whether the cell-body may become diseased and die without disease and death of the axone, or whether the axone may suffer or perish without destruction or involvement of the cell-body.

It must be shown whether a morbid process is always limited to a central or peripheral neurone, or whether degeneration passes from one to the other, from a motor to a motor neurone, or from a sensory to a sensory neurone, without any interference at the parts that have been regarded as points of contact of the neurones. It must be shown whether disease of a sensory neurone affects a motor neurone, or *vice versa.* To put the whole matter in a few words, we must obtain from pathology the evidence that what we recognize as a neurone suffers when diseased in so peculiar a manner that we may recognize in this involvement the individuality of the structure.

I shall not give a résumé of the pathology of the cell-body; that has been well done by capable investigators—van Gehuchten, Marinesco, Ewing, Barbacci, Robertson and others; but I shall endeavor to apply some of the literature on the subject and the results of my own investigations to the solution of the problems I have mentioned.

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[1] From the William Pepper Clinical Laboratory (Phœbe A. Hearst Foundation). Read at the twenty-sixth annual meeting of the American Neurological Association, May 1, 2, and 3, 1900.

We cannot deny that degeneration has a very evident tendency to involve distinct groups of nerve-cells, including their various processes. The existence of systemic diseases and of combined systemic diseases admits of little dispute, and we have in this limitation of morbid processes one argument in favor of neurones. Tabes, amyotrophic lateral sclerosis, Friedreich's ataxia and other diseases might be mentioned in illustration. It is not because all the axones affected in these diseases conduct impulses in one direction that they degenerate. We have in tabes, for example, a degeneration of posterior root fibers, including in some cases the descending roots of certain cranial nerves that are similar to the posterior roots of the spinal cord—the sensory fifth and the combined root of the ninth and tenth nerves—as I have seen in four or five cases. We do not have as a common finding in tabes degeneration of other ascending tracts; of the direct cerebellar or of the fillet. We have a selective degeneration of the primary sensory neurones, and a degeneration that does not as a rule pass to sensory neurones of another system. We have manifested in the pathological changes of certain systems an evidence of an individuality of these systems. I shall not dwell on this aspect of the subject lest I infringe on Dr. Sachs' rights.

We may inquire to what degree a neurone in its entirety becomes diseased. If we cut an axone, either central or peripheral, we know from the investigations of Nissl, Marinesco, van Gehuchten and many others that the cell-body in which this axone arises undergoes rapid alteration and possibly death, and that this alteration is probably more intense the nearer to the cell-body the division of the axone is made. Not only is the cell-body affected, but the central portion of the axone may also suffer more or less alteration. I need not refer to the degeneration of the peripheral end; that is well recognized as the degeneration of Waller. The earlier in the life of the animal the injury to the axone occurs the greater is the atrophy of the cell-body in which the axone arises. In a case of Pott's disease that I[2] studied the compression in the cervico-thoracic region probably began at the third year of the child's life, and by the eighth year the direct cerebellar tract *below* the compression and the cell-bodies in the column of Clarke had disappeared. I attach much importance to these findings, as I believe that mine was the first case recorded of complete atrophy of the cells of Clarke's column from a cervico-thoracic lesion.

Barker[3] in 1897 found *chromatolysis* in the cell-bodies of Clarke's columns in epidemic cerebrospinal meningitis, and explained it as a "reaction at distance."

Sano[4] in July, 1897, described *chromatolysis* of the cell-bodies of the column of Clarke, resulting from the pressure of a tumor on the direct cerebellar tract, the compression being chiefly at the fourth cervical segment. The alteration in Clarke's column consisted of central chromatolysis and some deformity of the nucleus. From the study of this case Sano concluded that the law of reaction at distance in a cell-body as a result of injury to its axone exists as truly for the central neurones as for the peripheral.

In my paper read in January, 1898, at the Johns Hopkins Hospital and published in June, 1898, I described complete destruction of the cell-bodies in Clarke's columns, and not merely chromatolysis, from a cervico-thoracic lesion.

Van Gehuchten[5] also has observed chromatolysis of these cell-bodies after the division of the spinal cord in the dog.

Sano,[6] in a later paper, reported the finding of chromatolysis in Clarke's column in six cases, resulting from lesions of the direct cerebellar tract.

I have become somewhat skeptical as to the value of chromatolysis in Clarke's column, and am inclined to think that these cells are especially liable to react in this way from many causes.

The change in the central end of the motor axone, apart from chromatolysis, after division of the axone has occurred, is not rapid, especially when the injury is at some distance from the cell-body. I have observed retrograde atrophy of the pyramidal fibers in several instances, but only when the transverse lesions were of long duration.

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[2] Spiller, The Johns Hopkins Hospital Bulletin, No. 87, June, 1898.
[3] Barker, Brit. Med. Journal, 1897, Vol. II, p. 1839.
[4] Sano, Journal de Neurologie, July 20, 1897, p. 276.
[5] Van Gehuchten, Journal de Neurologie, June 5, 1898, p. 238.
[6] Sano, Journal de Neurologie, Aug. 5, 1898, p. 313.

I have studied a case of peripheral nerve degeneration, the symptoms of which had existed for at least five or six years.

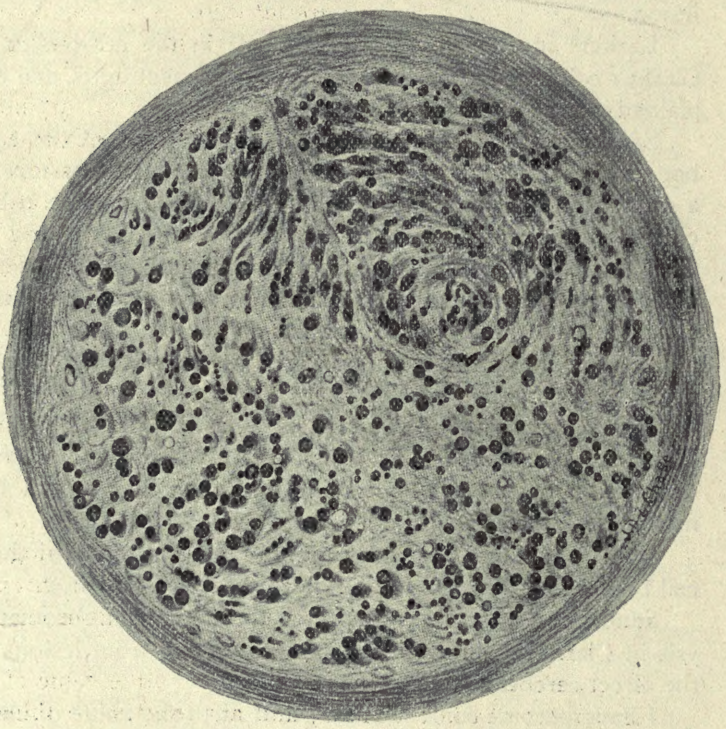

Fig I. Case of chronic neuritis of five or six years' duration. Nerve fibers of the left internal plantar nerve showing much degeneration. Some of the cell-bodies, from which the axones of this nerve arise, show the "reaction at distance" in the form of central chromatolysis and displacement of the nucleus.

The terminal portions of some of the branches from the sciatic show very distinct degeneration of the nerve fibers and overgrowth of the connective tissue in and about the nerve bundles. (Fig. I.). Many of the cell-bodies of the anterior horns of the lumbar region present central chromatolysis and displacement of the nuclei (Fig. II.), and this is in a case of chronic neuritis.

Nissl's stain is, of course, the most valuable for the study of nerve cells, but pronounced degeneration may often be told by the ammonium carmine stain. In my case of Pott's disease, to which I have referred, and in a case of acute poliomyelitis in an adult,[7] the destruction of cell-bodies was most evident by the carmine stain, and I am somewhat skeptical as to the importance of cellular changes that have existed many years, and cannot at all be detected by the carmine stain.

It seems that in acute diseases involving the axone, the cell-body in which the axone arises suffers, but if the disease becomes chronic, and is in the distal part of the axone, the cell-body may not show any serious alteration, even by Nissl's stain. The neurone as a whole suffers, but the chromatolysis may disappear, unless the degeneration involves a portion of the axone too near the cell-body. Dejerine and Thomas,[8] in a case of neuritis, found the nerves greatly altered without any appreciable change by the Nissl method in the cell-bodies in

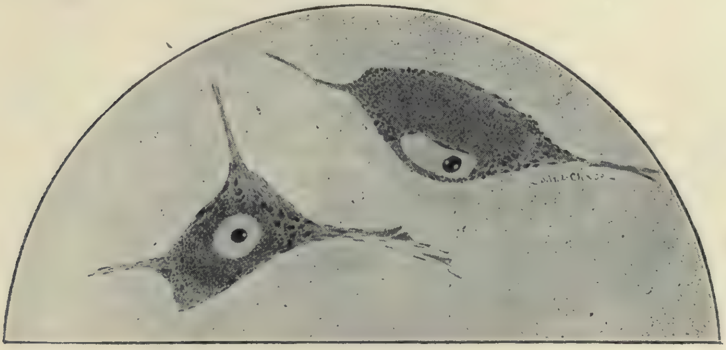

Fig. II. Chronic neuritis of five or six years' duration. The cell-bodies in the anterior horns in the lumbar region show the "reaction at distance."

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[7] Sherman and Spiller, The Philadelphia Medical Journal, March 31, 1900.

[8] Dejerine and Thomas, Comptes rendus de la Soc. de Biologie, 1897.

which these fibers arose. Cellular alteration, possibly, had occurred in this case, and the cell-bodies had recovered. The importance of chromatolysis is disputed. To Dejerine and Thomas it has little value, but to Schaffer it is an index of degeneration of a more essential portion of the cytoplasm. Dejerine[9] showed in 1889, by the examination of nine cases of tabetic muscular atrophy, that the peripheral nerves in their terminal portions were much diseased, and yet no cellular changes were found in the spinal cord. The Nissl method, of course, was not employed. If chromatolysis occurred in the cell-bodies in these cases—as it did occur in my case of chronic neuritis, the material from which I received from Dr. Mills; and in a case of facial paralysis of six months duration, now reported by Dr. Mills and myself (Fig. III.)—it had at least not led to atrophy of the cell-bodies.

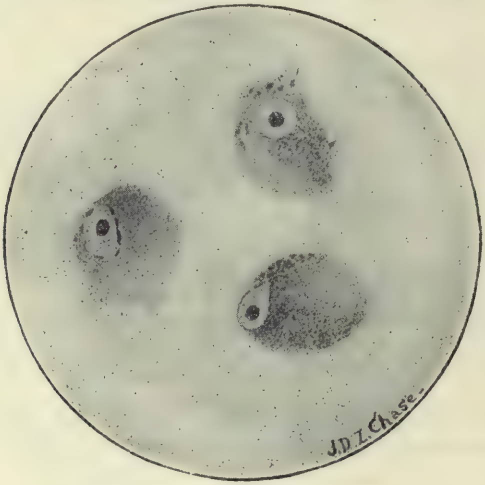

Fig. III. Cell-bodies of the facial nucleus in a case of peripheral facial palsy of six months' duration. A few of the cell-bodies within the nucleus are in a condition of almost complete chromatolysis, with displacement of the nucleus.

Van Gehuchten[10] holds that the restoration of a cell-body from chromatolysis occurring after division of the axone, is not dependent upon the reunion of the axone, and he refers to a similar statement made by Nissl. Van Gehuchten believes that reunion of the axone is without effect upon the restoration of the chromophilic bodies, but if restoration of the axone does not occur, the cell-body finally atrophies and disappears. Marinesco[11] advances somewhat different views. According to him the reparative process in a cell-body after its axone is cut is dependent upon the reunion of the axone, although both Marinesco and van Gehuchten seem to be in accord as to the final atrophy of the cell-body when the two ends of the axone remain ununited. Simple chromatolysis seems to me to be of doubtful value as indicative of cellular degeneration if, as van Gehuchten believes, it disappears, although the cell may die later, and is only a temporary reaction of the cell-body after division of its axone. Van Gehuchten has been unable to obtain even temporary chromatolysis in the spinal cell-bodies of rabbits and dogs by cutting the axones of these cell-bodies, but with de Buck,[12] he has found chromatolysis in the spinal cord of man after amputation of a limb. Chromatolysis in man after amputation of a limb has been observed also by Flatau[13] and by Sano.[14] I have had the rare good fortune to obtain the spinal cord from a case in which amputation at the hip joint was followed by death after five and a half days. The cell-bodies in the lumbo-sacral region on the side of the amputation have undergone great chromatolysis, and in some of the cell-bodies displacement of the nucleus has occurred. The cell-bodies in the anterior horn of this side stain very faintly. On the other side of the cord the cell-bodies of the anterior horn are much more deeply stained, although some of them show chromatolysis. The difference in the condition of the cell-bodies of the two horns is striking. The chromatolysis in many cell-bodies is complete; in others, it is merely central.

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[9] Dejerine, "Sur l'atrophie musculaire des ataxiques," 1889.

[10] Van Gehuchten, "Anatomie du système nerveux de l'homme," third edition, Vol. 1, 1900, and Presse méd., 1899, p. 3.

The neurone in all its parts is not always promptly affected when the cell-body is seriously diseased. The case of acute poliomyelitis reported by Dr. Sherman and myself (*l. c.*), is an evidence of this. The disease was of short duration, but was sufficiently long to cause destruction of the cell-bodies of the anterior horns, and to leave the motor roots unaffected, not even causing swelling of the axones. I could refer to a number of similar cases in literature. In the case of hemorrhagic pachymeningitis reported to this Association last year by Dr. McCarthy and myself,[15] intense alteration of the cell-bodies was observed, but none of the axones. If the objection should be raised that this cellular change was recent, and possibly from edema, and therefore alteration of the axones had not time to develop, I would reply that precisely the same changes were observed by Hirsch,[16] in a case of amaurotic family iodiocy, and that this observation by Hirsch and the improbability of an edema of *recent* origin in our case, would lead me to believe that the cellular changes throughout the central nervous system probably were not recent. The changes in Hirsch's case could not have been of post-mortem origin, as the necropsy was made four hours after death. In his case, however, the change in the cell-bodies was associated with degeneration of the pyramidal tracts, and in ours it was not. I have recently studied another case in which the same cellular changes existed, and degeneration of the pyramidal tracts did not occur. This was a case with the symptoms of meningitis in a feebleminded child. Cellular changes such as those just described I have been unable to find in cortical edema.

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[11] Marinesco, Presse méd., 1898, pp. 201-206.

[12] Van Gehuchten and de Buck, Journal de Neurologie, 1898, p. 94.

[13] Flatau, Deutsche med. Wochenschrift, 1897, p. 278.

[14] Sano, Journal de Neurologie, 1897.

It would seem, therefore, that the cell-body, though greatly altered morphologically, is still capable of exerting an influence on the health of the axone, and that so long as the cell-body persists and is not too seriously altered, the axone may live. An axone is only partially dependent upon the cell-body for its vitality, and if the blood supply to it at a considerable distance from the cell-body is cut off, that portion deprived of the circulation dies, but the cell-body seems to be necessary to the axone to enable it to appropriate the nourishment brought to it.

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[15] Spiller and McCarthy, The Journal of Nervous and Mental Disease, 1899, p. 677.

[16] Hirsch, The Journal of Nervous and Mental Disease, 1898, p. 538.

Diseases that are due to poisons also have a decided tendency to affect certain neurones in their entirety, as was evident in the case of Landry's paralysis reported by Dr. Mills and myself,[17] in which only the peripheral motor neurones were affected. Similar cases are reported in literature.

Central motor neurones degenerate in a manner very like that of the peripheral motor neurones. Marinesco[18] found very intense alteration of the cells of Betz, and only of these cells, in the paracentral lobule, following a lesion of the internal capsule. These large cell-bodies may entirely disappear, as the result of such a lesion. The cellular changes consist of tumefaction of the cell-body, chromatolysis and alteration and displacement of the nucleus. Marinesco thus confirms the statement of v. Monakow,[19] that the large pyramidal cell-bodies of the paracentral lobule disappear after destruction of the internal capsule. From the integrity of the other cell-bodies of the paracentral lobule, Marinesco seems to conclude that these smaller cell-bodies do not give origin to motor fibers. His words in speaking of the cells of Betz are: "Ce sont ces cellules qui donnent naissance aux fibres pyramidales." As the large cells of Betz are scarce in the lower portions of the motor cortex, we may hesitate to accept the view that Betz's cells are the only ones in the motor cortex that are motor in function. Marinesco refers to the fact that Dotto and Pusateri have seen cellular changes in the motor cortex following destruction of the internal capsule.

Ballet and Faure[20] found that after the fibers of projection from the motor area were cut, the motor cortical cell-bodies atrophied. The cellular changes were similar to those that occur in the motor cell-bodies of the cord when the peripheral motor fibers are divided. They experimented on seven dogs, and presumably made the division of the fibers not far below the cortex. The point of attack is of importance in the production of cellular lesions, as the nearer the interruption of the axone is to the cell-body, the greater is the alteration of the cell-body.

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[17] Mills and Spiller, THE JOURNAL OF NERVOUS AND MENTAL DISEASE, 1899.

[18] Marinesco, Revue neurologique, 1899, p. 358.

[19] Von Monakow, "Gehirnpathologie," p. 118.

[20] Ballet and Faure, Semaine méd., 1899, p. 109.

I have studied the paracentral lobule in five cases of capsular lesion, three of which were due to hemorrhage of various durations, but I have been unable to convince myself that characteristic changes occurred in the cells of Betz. I have been more fortunate in my examination of the cortex in cases of long duration. One of the brains studied was from a half-grown boy who had survived for ten or eleven years the closure of the left Sylvian artery. The motor area was destroyed except in its extreme upper portion. The motor axones from this area were cut near their origin. Very few cell-bodies were found in the paracentral lobule, and the cells of Betz were almost entirely absent. The sections from the paracentral lobule of this brain were exceedingly interesting in comparison with those from the paracentral lobule of a brain in which the lower part of the left motor area was destroyed by porencephaly. The motor axones above this lesion were not injured so close to the cell-bodies. The porencephaly naturally suggests a congenital lesion, and the motor axones from the upper left motor area were probably arrested in their downward growth. The results were similar to those produced by dividing the axones. As the lesion was not so near the cell-bodies of origin in the paracentral lobule as in the former case, fewer cell-bodies had disappeared entirely, and yet those present were much below the normal number, were small and rounded, the pericellular spaces were large, and the cells of Betz seemed to be absent. These two cases have given results very like those obtained experimentally by Ballet and Faure, only the cellular changes in my cases were much more intense. Destruction of the cells of Betz from cerebral lesions have been observed not only by v. Monakow, but also by Moeli, Henschen, and Mahaim.

The peripheral sensory neurone reacts in a peculiar way to traumatism. It is very remarkable that, while division of the peripheral process of a spinal ganglion cell-body causes very distinct degeneration of this cell-body (Lugaro, Mering, Fleming, van Gehuchten, Cassirer), and even complete destruction of the cell-body according to some, division of the central process causes no cellular reaction. This is a very interesting statement and of much value in the explanation of tabes. Marinesco [21] denies that the cell-body of the peripheral sensory neurone dies when its peripheral process is cut, as van Gehuchten believes.[22]

Cassirer[23] has found that after a peripheral nerve is cut a large number of cell-bodies in the spinal ganglion belonging to this nerve degenerate, but only a few are so greatly altered that they probably undergo complete destruction. As a result of this cellular degeneration he finds that a moderate degeneration of posterior roots occurs. The changes which Cassirer found in the posterior roots as a result of the division of the peripheral nerve were slight, as they were also in some similar experiments performed by Redlich, and therefore Cassirer thinks his findings afford no support for the theory that tabes begins in the peripheral nerves. There is no comparison, he thinks, between the slight degeneration of the posterior roots when a whole nerve is cut and the intense degeneration of these roots in tabes.

In a Gasserian ganglion removed recently by Dr. Harvey Cushing for trifacial neuralgia I found alteration by Nissl's stain in quite a number of the cell-bodies of the ganglion—by no means the majority, however—but was not able to detect any change in the sensory root, although I found alteration of the sensory root in another ganglion removed by Dr. Cushing. Krause[24] also reports disease of a sensory root. My examination of the ganglion referred to and of its sensory root has given results similar to those obtained by Cassirer and Redlich in experiments on the spinal ganglia, *i. e.*, alteration of cell-bodies of the ganglion with little alteration of the cellulifugal processes.

The destruction of the spinal ganglion was very much less in Cassirer's experiments than in those of Lugaro and van Gehuchten, and therefore we might expect slight alteration of the posterior roots in Cassirer's cases. It seems impossible to examine a picture in which the cells are as few in number as in that given by van Gehuchten[25] on p. 335 of the recent edition of his text book, and to believe that the cellulifugal processes of the cell-bodies of the ganglion in such a case were only slightly degenerated.

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[21] Marinesco, Presse méd., 1898, p. 201.

[22] Van Gehucten, "Anatomie du système nerveux de l'homme," third edition, Vol. 1, 1900.

[23] Cassirer, Deutsche Zeitschrift für Nervenheilkunde, Vol. 14, p. 150.

[24] Krause, "Die Neuralgie des Trigeminus," Leipzig, 1896.

Schaffer's[26] finding of normal cell-bodies by the Nissl method in the spinal ganglia in tabes is a further proof that the cell-bodies of the spinal ganglia do not react promptly to lesions of their central processes. I also in the examination of a case of tabes by Nissl's stain have found the cell-bodies in the spinal ganglia of the lumbar region normal.

We see, therefore, that on the whole there is a tendency for the entire neurone to undergo alteration when it is attacked by disease or injured experimentally, but that a portion may be more resistant than the rest and may recover even though at first affected, although the end in union with the cell-body may finally atrophy. The earlier in life the lesion occurs the less is the resistance of the neurone. From these facts we have some evidence of the individuality of the neurone.

A very interesting question is in regard to the degree of limitation of degeneration to one set of neurones, either sensory or motor. It is quite certain that a restriction exists, but occasionally this restriction is overcome. Tertiary degeneration —and by that I mean a degeneration in another series of neurones resulting from secondary degeneration of a series of neurones nearer the origin of the impulses—does not seem to be of very frequent occurrence. It is important to make a distinction in regard to this matter. The changes that occur in a second neurone associated with *primary* degeneration in a first neurone—and by that I mean degeneration not due to a focal lesion—cannot be compared with the degeneration of one neurone following degeneration of another from a focal lesion. In the first instance we have reason to believe that the first neurone that undergoes primary degeneration does so as a result of imperfect development, or possibly as the result of the action of a poison, and we do not know that the same causes have not produced the degeneration of the second neurone. In amyotrophic lateral sclerosis, for example, of which I have studied the specimens of two cases, we have no proof that the degeneration of the peripheral motor neurones is the result of degeneration of the central motor neurones, or *vice versa.*

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[25] Van Gehucten, "Anatomie du système nerveux," third edition, Vol. 1.

[26] Schaffer, Neurologisches Centralblatt., 1898, p. 2.

I have examined cases of hemiplegia in the adult with sclerosis of the pyramidal tract, but have never seen degeneration of the cell-bodies of the anterior horns by the carmine stain and of the nerve fibers arising from them, *i. e.,* I have not found tertiary degeneration in these cases. In my case of Pott's disease of early development, to which I have referred, in which both pyramidal tracts were destroyed, the cell-bodies in the anterior horns in the lumbar region by the carmine stain were normal in shape and size, the dendritic processes were not entirely perfect, the nuclei were central and the cells were normal in number. This was an excellent case for the study of tertiary degeneration, as the lesion occurred at the third year of life, and the cell-bodies of Clarke's column had disappeared as a result of retrograde atrophy, but tertiary degeneration if it existed had not caused much alteration.

I have examined by the carmine stain a case of spinal hemiplegia from a lesion in the cervical region which had existed for a number of years. The cell-bodies in the lumbar region on the side of the degenerated crossed pyramidal tract were numerous, the nuclei were central, but the dendritic processes were possibly not perfectly developed.

Of course the cells in both these cases might have shown some alteration if Nissl's method had been employed, but I chose two cases of lesion of the lateral columns in the cervical region to show that atrophy of the cell-bodies of the anterior horns detectable by carmine does not occur to any extent from degeneration of the lateral columns. Possibly a lesion developing even earlier than the third year of life might give different results, or I might have obtained chromatolysis by Nissl's method in these cases. I have recently obtained a spinal cord which was greatly compressed in the upper cervical region by an intradural tumor. The patient had been paralyzed in all the extremities. Many of the cell-bodies in the anterior horns of the lower cervical region are much diseased and are in a condition of central chromatolysis and vacuolation with displacements of the nucleus (Fig. IV.). In the lumbar region the altered cell-bodies are much less numerous. This is possibly tertiary degeneration, but some of it may be "reaction at distance" from the injury of the axones of cells located lower in the cord.

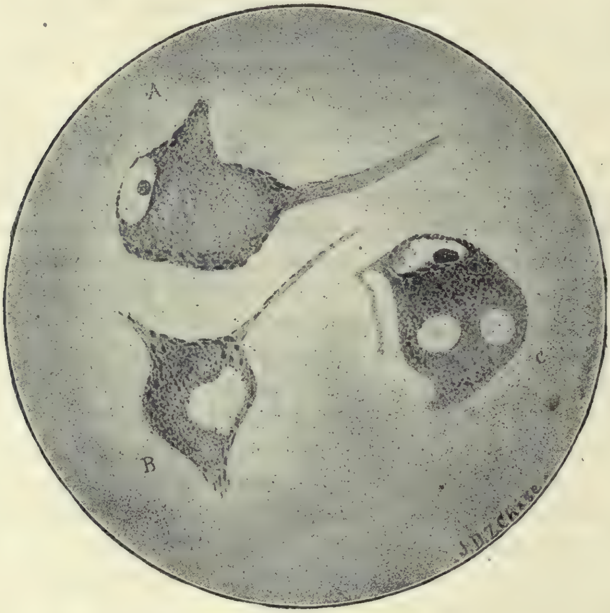

Fig. IV. Cell-bodies of the anterior horns in a case of tumor of the upper cervical region. Many of the cells show central chromatolysis and vacuolation. Cell-body A is from the lumbar region, B and C from the lower cervical. The cellular changes may be "reaction at distance" from injury of the axone, or may be tertiary degeneration of the peripheral motor neurone.

I am at present studying a case of very great value—one of cerebral diplegia from an unilateral lesion. The history is imperfect, but it is positively asserted by thoroughly reliable persons that four and a half years before the boy's death he had been able to walk, but his gait was probably not normal.

He soon lost this power after he came under observation, and his limbs became helpless and contractured. I found intense internal hydrocephalus limited to the right hemisphere, and this hemisphere was a thin-walled sac. The motor fibers were greatly injured and the left crossed pyramidal tract was sclerotic, and yet the cell-bodies in the anterior horns of the cervical and lumbar regions seemed to be normal in number, and little change could be detected by Nissl's method. The boy was fourteen years old when he died. Surely this was a very suitable case for testing tertiary degeneration in the peripheral motor neurones.

Schaffer,[27] however, has observed chromatolysis of the spinal motor cell-bodies in recent hemiplegia, and this chromatolysis was especially noticeable in the postero-lateral group. Quite different are the results obtained by Marinesco.[28] In sixteen cases of hemiplegia with degeneration of the pyramidal tract, that he examined, he found alteration of the cell-bodies in the anterior horns of the cord only in three, and in two of these cases the altered cell-bodies were not numerous and might easily have escaped detection. In the case in which the changes were distinct they were like those seen when an axone is cut, and were suggestive of neuritis.

We should be exceedingly cautious in accepting diminution in the size of one anterior horn as a result of degeneration of the pyramidal tract. In the case of malaria of the central nervous system, the report of which I present at this meeting, a slight sclerosis existed in one crossed pyramidal tract and the anterior horn on that side throughout the cord was distinctly smaller than the horn of the other side. The number of the cell-bodies was about the same on the two sides. The sclerosis, was so slight and the symptoms it caused so transient, that I look upon the diminution in size of the anterior horn occurring with the slight sclerosis of the motor tract merely as a coincidence.

Berger[29] has found very distinct degeneration of the cell-bodies of the anterior horns in paretic dementia. This degeneration might have been regarded as due to toxic causes or to degeneration of the pyramidal tracts. The experiments Berger performed are of much interest in the light of Warrington's[30] positive findings. Berger was unable to produce in the dog degeneration of the contralateral anterior horn cell-bodies by destruction of the motor cortex, although the pyramidal tract in the cord was degenerated. In another dog he destroyed the cortical motor area and divided the contralateral posterior roots and allowed the animal to live four weeks. The cell-bodies of the anterior horns were not degenerated. In a cat in which the pyramidal tract of one side had been destroyed for two years no cellular changes in the corresponding anterior horn were found. Dr. McCarthy, at my request, has kindly cut for me posterior roots in three cats. One cat was allowed to live seven days, another nineteen days, and the third twenty days. The examination of the spinal cord from these animals has given results similar to those obtained by Berger. I find no distinct alterations of the cells of the anterior horns resulting from division of the posterior roots.

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[27] Schaffer, Monatsschrift für Psychiatrie und Neurologie, Vol. 2, No. 1.

[28] Marinesco, Semaine méd., 1898, p. 465.

[29] Berger, Monatsschrift für Psychiatrie und Neurologie, Vol. 3, p. 1.

The results of these experiments cannot be applied equally well to man. The dog and cat seldom use one limb separately, and probably all four limbs are innervated from both sides of the brain more nearly equally than they are in man. To cut off the stimulation from the cortex in the dog it would be necessary to destroy both motor tracts, and possibly even then this would not be sufficient on account of the existence of "extra-pyramidal" tracts.

I have re-examined the sections in the case of syringomyelia reported by Dr. Dercum and myself[31] before this Association four years ago. The posterior horn of the right side was destroyed from the first thoracic segment throughout the cervical region, and in the lower part of the cervical region the crossed pyramidal tract on the side of the destroyed posterior horn exhibited distinct retrograde atrophy. The lesions had existed for a number of years and the cells of the right anterior horn had been deprived of all stimulation through the right posterior cervical roots, and to some extent of the stimulation from the brain through the right motor tract of the cord, on account of the retrograde atrophy of the right crossed pyramidal tract. There may possibly be a slight decrease in the number of cell-bodies in the right anterior horn, but this decrease is questionable and the cell-bodies present appear to be normal by the carmine stain, and have well-developed dendritic processes and central nuclei. The case does not give any positive evidence of degeneration of the cell-bodies of the anterior horn from lesions of the posterior roots.

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[30] Warrington. Journal of Physiology, Vol. XXIII.

[31] Dercum and Spiller, The American Journal of the Med. Sciences, 1896.

Degeneration of the peripheral motor neurone certainly may exist at least many years without degeneration of the central motor neurone. I refer in proof of this statement to the interesting and much cited case reported by Senator. The symptoms of amyotrophic lateral sclerosis existed for about five years, and Senator[32] found a pronounced simple, non-inflammatory atrophy of the cell-bodies in the anterior horns of the cervical and thoracic regions. The anterior roots were not distinctly diseased. He says positively that lateral sclerosis was *entirely* wanting.

Dejerine's[33] cases are further proof in this respect. In two cases of progressive spinal muscular atrophy the peripheral motor neurones were intensely diseased, but absolutely no degeneration of the pyramidal tracts was detectable. One case lasted eighteen years and the other ten years. These specimens Dr. Dejerine has permitted me to study. Similar cases have been reported by Dreschfeld, Oppenheim, Nonne, Dutil and Charcot.

I have never seen involvement of the lemniscus as a result of degeneration of the posterior columns. Two cases in literature in which this was reported occur to me. One was a case reported by Schaffer[34] and is of most difficult interpretation; the other is by Rossolimo.[35] In the latter the portion of medulla oblongata containing the nuclei of the posterior columns was not examined, and these nuclei may have been altered independently of the degeneration of the posterior columns. I have traced intense degeneration by Marchi's method from the sacral cord to the nuclei of the posterior columns, but never beyond.

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[32] Senator, Deutsche med. Wochenschrift, No. 20, 1894, p. 433.

[33] Dejerine, Comptes rendus de la Soc. de Biologie, 1895, p. 183.

[34] Schaffer, Archiv für mik. anatomie, Vol. XLIII.

[35] Rossolimo, Archiv für Psychiatrie, Vol. XXI.

Schaffer[36] thinks that the degeneration of the direct cerebellar tract in tabes is an example of the influence of peripheral sensory neurones on central sensory neurones. I know such cases have been reported, but I have never been fortunate enough to observe any, although I have examined many cords from tabetic persons. I think, therefore, that this degeneration must be rare. Schaffer, however, can give no example of the influence of a central sensory neurone upon a peripheral sensory neurone. He has found central chromatolysis and displacement of the nuclei in the cell-bodies of the anterior horns in tabes and he attributes these cellular changes to the degeneration of the sensory roots. The changes, however, may be due to the peripheral neuritis occuring in tabes. I also have seen this chromatolysis of the cells of the anterior horns in tabes.

A statement made by van Gehuchten is of no value as evidence of tertiary degeneration. Van Gehuchten[37] observed chromatolysis of the terminal nucleus of the acoustic nerve after division of the nerve, and reported this finding at the meeting of the Congress in Moscow. He explained this chromatolysis by the theory of Marinesco and regarded it as the result of injury of the first neurone and of loss of irritation normally conveyed by this neurone. Further researches convinced him that his technique was at fault. The view he now holds is that division or injury of a peripheral sensory nerve does not cause early changes in the cell-bodies forming the terminal nucleus of this nerve. He has not, therefore, seen chromatolysis in the terminal nucleus as a result of injury to the peripheral sensory neurone.

I know of no positive evidence that disease of a sensory neurone ever results from disease of a motor neurone.

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[36] Schaffer, Monatsschrift für Psychiatrie und Neurologie, Vol. 3, p. 64.

[37] Van Gehuchten, Journal de Neurologie, Nec. 20, 1898, p, 502.

I am, of course, well aware of Marinesco's[38] views. He teaches that every disturbance of function in a neurone affects the function of the neurone with which it is in connection. Lesion of a sensory neurone causes in course of time alteration of a second sensory neurone of a different series, possibly even of a sensory neurone of a third series. Lesion of the cortical substance causes similar neuronic atrophies, but in an opposite direction. This theory sounds so plausible that we cannot reject it, but my researches cause me to believe that the influence of one neurone upon another has been to some extent exaggerated.

I would not give the impression that tertiary atrophy—I use the word atrophy and not degeneration—does not occur. I believe that when the function of a neurone is destroyed early in life, even though the neurone is not directly injured as, for example, by division of its axone, this neurone whose function has been arrested develops very imperfectly or possibly even atrophies. The diminution in the size of the lateral column following amputation of a limb is regarded as an evidence of this, and I have seen slight diminution of the anterolateral column following early amputation. Tertiary degeneration in the adult—possibly it is never more than atrophy—I believe to be rare, especially in the motor system. Tertiary atrophy is possibly more common in the sensory system or in the visual tract, and possibly the explanation of this difference lies in the fact that the peripheral motor neurones are under the stimulation of both the pyramidal tracts and of the sensory roots.

The fact that two neurones in connection with one another do not degenerate to the same degree and with the same rapidity from one lesion is evidence that there is some difference in structure at the point where they come together, and that the essential elements of one neurone are not the same essential elements of another neurone.

That degeneration may occasionally pass from one neurone to another is no proof that neurones do not exist. It is certainly not common for systemic diseases to spread irregularly to neighboring areas. The views of Held, Apáthy, Bethe and Nissl may force us to modify our conceptions of the neurone, but the evidence offered by pathology of the existence of neurones, *i. e.*, of structures having a functional individuality, will have to be harmonized with the results of anatomical studies.

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[38] Marinesco, Presse méd., 1898, p. 201.

PATHOLOGICAL REPORT ON A CASE OF DERMATITIS VESICULO-BULLOSA ET GANGRÆNOSA MUTILANS MANUUM (DUHRING), WITH A CONSIDERATION OF THE RELATIONS OF VASCULAR AND NERVOUS CHANGES TO SPONTANEOUS GANGRENE AND RAYNAUD'S DISEASE.[1]

By WILLIAM G. SPILLER, M.D.

(From the William Pepper Clinical Laboratory, Phoebe A. Hearst Foundation.)

PLATES IV AND V.

This case was reported clinically by Dr. L. A. Duhring[2] in 1892 under the title of a "Case of Dermatitis Vesiculosa Neurotraumatica of Forearm." Dr. Duhring thought that the case was obscure and difficult to classify, and notwithstanding the presence of hysteria he believed that the symptoms could possibly be explained by regarding the process as a traumatic ascending multiple neuritis, although he was guarded in expressing this view.

A later clinical history was published by Dr. Sinkler[3] in 1897, in which much of the earlier history given by Dr. Duhring is included. A brief abstract of Dr. Sinkler's paper is as follows:

The woman, A. A., was 35 years of age in 1897. For years she had had many symptoms of general nervous disorder which included frequent and protracted attacks of gagging and vomiting, palpitation of the heart, crying spells and globus hystericus. In Sept., 1890, she was burnt with a flat-iron on the flexor surface of the left forearm just above the wrist, the area being about the size of a silver dollar. The burn was superficial but did not heal readily or completely, and from some unknown cause began to break out anew. Within a month of the accident it began to show a superficial gangrenous patch which remained about six weeks. The whole forearm became reddened and the seat of throbbing and darting pain. About six weeks after the accident the burn seemed to be nearly healed, and then a single pimple, a papulo-vesicle, formed on the extensor surface of the forearm near the burn. In a week or two this lesion ulcerated and crusted, and then other similar pimples formed near the original one; some of them vesicles and some blebs, covering by degrees the greater portion of the wrist. The morbid process continued on the left wrist and upper part of the hand for three years, migrating from place to place and breaking out anew as soon as any point became healed. By the early part of 1894 the left arm was entirely healed.

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[1] Read before the Section on Neurology and Medical Jurisprudence of the American Medical Association, June 5, 1900.

[2] *International Medical Magazine*, 1892, i, p. 140.

[3] *Journal of Nervous and Mental Disease*, 1897, xxiv, p. 687.

Just at the time of the healing of the left arm a papulo-vesicle similar to those which had invaded the *left* arm appeared at the end of the *right* index finger. This followed the same course of breaking out into an ulcer and then healing; new papulo-vesicles formed on this finger and then attacked the adjoining fingers. The affection subsequently spread to the dorsal and palmar surfaces of the hand and finally implicated all of the fingers. At times gangrenous patches appeared on the fingers, followed by sloughing and more or less loss of tissue. In this way the fingers and thumb were lost. The patient suffered from pain in the right hand. Objective sensation was unimpaired. The sloughing began with discoloration of the skin and the skin rapidly became black and dry and the slough was thrown off leaving a granulating surface. The urine was free from sugar.

Dr. Sinkler concluded after a careful study of the case that the disease was a trophoneurosis dependent upon an hysterical diathesis.

I made a brief examination of the patient in June, 1899, and observed certain symptoms that caused me to believe that the woman had Graves' disease. I made no notes of her condition, knowing that the case had been studied clinically by Dr. Duhring and Dr. Sinkler. Dr. Sinkler later informed me that the patient had marked evidences of Graves' disease; at least she had distinct exophthalmos and rapid heart's action without much, if any, thyroid enlargement.

In June, 1899, the right hand was amputated by Dr. W. J. Taylor just above the wrist and was given to me for examination (see Plate IV, Fig. 1). The part had become useless and pus had formed in the stump of the fingers. Dr. Sinkler tells me that the patient had been for years an opium eater. After the amputation she did very well and was improving steadily when one day she received a large quantity of opium pills from some friends. She probably took several of these, as in the evening after the visit of her friends she vomited and was found in a condition of stupor. The next morning she had a convulsion. The urine was examined but no evidence of nephritis was obtained. The convulsions became more frequent, the stupor continued, and she died on the third or fourth day after taking the opium.

Previous to her death Dr. Duhring[4] published another clinical report of this patient and a beautiful colored drawing of the right hand.

Dr. C. W. Burr made the necropsy and kindly placed at my disposal the brain, cord and some of the peripheral nerves.

Dr. Joseph Walsh made a bacteriological examination of the amputated hand. Important results were not expected from this examination as the parts were exposed to various kinds of infection. His report is: "Aërobic and anaërobic cultures were made from suppurative foci on the fingers and hands and from non-suppurative portions. The results were positive and pure cultures of staphylococci were obtained, the great majority being white staphylococci. Inoculation into guinea-pigs of pus from the suppurating foci and of the pure cultures in agar produced no effect."

The microscopical examination of the tissue was made by me.

Right upper extremity: Ulnar nerve and artery.—The ulnar artery taken from the amputated limb is much thickened, both in the media and intima, especially in the latter. The lumen at one part is almost entirely filled by an organized thrombus (see Plate IV, Fig. 2). An elastic membrane is seen along one side of this thrombus. This thrombus is separated from the intima by a clear space throughout most of its extent.

The nerve fibres of the ulnar nerve in the same section in which the thrombosed ulnar artery is found, appear to be normal by ammonia carmine and the Weigert hæmatoxylin stains. The ulnar artery towards its peripheral terminations is still much thickened, and yet the nerve fibres of the accompanying nerve are normal by ammonia carmine or

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[4] *International Atlas of Rare Skin Diseases*, xiv, March 22, 1899.

Weigert's hæmatoxylin stain, or at most are very slightly altered. A section of the ulnar nerve taken from the amputated limb and stained by Marchi's method shows only a moderate amount of black masses within the nerve fibres, and it is questionable whether the nerve could be regarded as degenerated from the evidence furnished by this method.

Nerve fibres from the right hand—I cannot say which nerve—taken just above the finger and stained in the fresh state by osmic acid and teased appear to be normal. The same is true of nerve fibres taken from the lower third of the right forearm.

Median nerve.—A piece of the median nerve, taken about 8 cm. above its termination in the stump, shows some proliferation of the endoneurium with possibly an atrophy of some of the nerve fibres. The extreme end of the branch to the middle finger is considerably degenerated and the endoneurium is much proliferated. Many nerve fibres have disappeared and the small accompanying arteries are much thickened. The extreme end of the branch to the index finger shows some degeneration of the nerve bundles. The extreme end of the branch to the thumb shows distinct degeneration of nerve fibres and proliferation of the endoneurium, but many nerve fibres are still present.

A section from the median nerve of the amputated hand and forearm stained by the Marchi method shows degeneration in some of the nerve fibres, but the degeneration is not excessive and is not so great as that seen in the left brachial plexus. Masses stained black by the osmic acid are seen in many of the fibres.

Radial nerve.—The radial nerve from the amputated part, taken 6 cm. above the styloid process of the radius, shows distinct diminution in the number of nerve fibres and overgrowth of the endoneurium (see Plate V, Fig. 3), but the degeneration is slight in comparison with that of the distal portion of the branch to the thumb. With the Marchi stain the degeneration 6 cm. above the styloid process is considerable. At the distal portion of the branch of the radial nerve to the thumb (Plate V, Fig. 4) the alteration of the nerve fibres is greater than in any other nerve. The fibres here have mostly disappeared and the connective tissue is greatly proliferated.

A branch of the radial artery taken just above the thumb and 4 cm. below the styloid process of the radius may be regarded as normal, although the radial artery examined 8 cm. above the styloid process shows distinct, but not excessive overgrowth of the intima, this being considerably less than that seen in the ulnar artery.

Right brachial plexus.—The brachial artery and the nerve fibres appear to be normal by Weigert's hæmatoxylin stain and the ammonia carmine, and the degeneration is unimportant by the Marchi method.

A vein taken from the back of the right hand shows some proliferation of the intima.

Left upper limb.—A small portion of the radial nerve and a portion of the brachial plexus were the only tissues of this extremity placed at my disposal for study.

The left radial nerve at a point unknown to me shows as distinct a diminution of nerve fibres and proliferation of the endoneurium as does the right radial 6 cm. above the styloid process.

The intima of the left brachial artery is slightly thickened. The nerve bundles of the plexus by the ammonia carmine stain are normal and yet the Marchi method shows a very intense degeneration of the myeline, which must have been recent—a greater degeneration indeed than is seen in any other nerve except perhaps the right radial. In the left brachial plexus in certain nerve bundles are a few areas in which no nerve fibres exist and only loose fibrous connective tissue is found. These areas are sharply defined from the surrounding nerve fibres of the bundle. In one bundle two such areas are seen. It is impossible to say whether these are imperfections in the original development of the tissue or the result of degeneration of nerve fibres.

Muscle.—The first interosseous muscle of the right hand is not much altered. The muscular fibres are nearly normal in size. The larger intramuscular nerve bundles are wonderfully well preserved, although the smaller bundles show some proliferation of the endoneurium. The intima and media of some of the small vessels within this muscle are thickened.

The skin from the back of the hand just above the fingers has lost the epidermis and the papillæ of the cutis vera are flattened.

Spinal cord.—Sections were taken for microscopical study from the lower cervical and upper thoracic regions and were found to be normal. Nissl's method could not be employed as the spinal cord had been put in Müller's fluid. Some of the motor cells of the anterior horns are vacuolated, but the cells have normal processes and do not appear to be atrophied. Cells found in the area corresponding to Clarke's columns are not atrophied, and so far as can be determined by the carmine stain they are normal. The nuclei in some are eccentric.

The medulla oblongata is normal. The brain by macroscopical examination is normal.

The lesions in this case in brief are as follows: The central nervous system is normal. The nerves in the distal portion of the right hand near the metacarpo-phalangeal articulations are much altered, especially the radial; the ulnar less distinctly so. The right median nerve is slightly altered at about 8 cm. above its terminal portion in the stump of the hand, and the right radial 6 cm. above the styloid process is somewhat degenerated. The nerves could not be studied at higher levels, as the tissue necessary for this was not in my possession. The right brachial plexus is normal. The ulnar nerve is normal except in its most distal portion where the alteration is slight.

The arteries of the right upper limb are diseased in some parts. The ulnar artery near the wrist shows the greatest amount of thickening of the intima and at one portion an organized thrombus is found. The right radial artery shows some proliferation of the intima.

The brachial plexus of the left side gives evidence by Marchi's method of intense recent degeneration, but this is not seen by the ammonia carmine stain. The intima of the left brachial artery is slightly thickened. The left radial nerve is not entirely normal.

It does not seem probable that the vascular changes alone could have produced the peculiar trophic lesions of the right upper limb. Even the organized thrombus of the right ulnar artery had not caused degeneration of the accompanying nerve, and the changes in the right radial artery were not very important. The slight alteration of the ulnar nerve in its most distal portion was probably the result—as was the alteration in the other nerves of the hand—of spontaneous amputation and gangrene, and not of thrombosis of the ulnar artery. The veins had not escaped. The nerves of the right upper limb were seriously diseased only at their terminations near the gangrenous area, except perhaps the radial which was diseased at least 6 cm. above the styloid process of the radius. It is questionable whether so extensive lesions can be explained by so slight degeneration of nerves.

Where peripheral gangrene occurs and the vessels and nerves of the gangrenous limb are found diseased several questions are at once suggested;

1. Was the gangrene caused by the endarteritis obliterans?

2. Was the gangrene caused by the degenerative changes in the nerves?

3. Was the degeneration of nerves and vessels the result of the gangrene?

4. Were the nerve lesions the result of vascular disease?

5. Was the degeneration of the vessels produced by the changes in the nerves?

These questions can be best answered by a study of the cases reported in literature, and they will be considered seriatim.

Raynaud[5] began one of his papers on symmetrical gangrene with a quotation from a work of Victor François written in 1832: "Everything concerning spontaneous gangrene is in a state of distressing uncertainty." These words are not quite so true as they were at the time they were first written, but much of this "distressing uncertainty" still remains. Cases of gangrene in which the cause cannot be determined are still reported as shown by an interesting paper by McFarland.[6]

1. *Can gangrene be caused by endarteritis obliterans?*

Many cases have been reported in which obliterating endarteritis was believed to be the cause of gangrene. The description of the "gangræna ex endarteriitide hyperplastica" as given by Billroth represents the disease as beginning with prodromal symptoms lasting many years, viz., disturbance of circulation, cyanosis of the limbs, a sensation of cold and weight, paræsthesia, and inability to stand long or walk far. The gangrene is produced by a slight cause and is usually moist.

Von Winiwarter[7] concluded from his examination of several cases of so-called primary, spontaneous gangrene that the underlying cause is an endarteritis terminating in complete closure of the affected vessels. Zoege von Manteuffel[8] finds that this form of endarteritis is the result of successive deposition and subsequent organization of layers of thrombi, so that finally the lumen of the vessel becomes filled with vascularized connective tissue, and Hoegerstedt and Nemser[9] believe that in general thrombosis participates in a similar way in the production of obliterative endarteritis. Haga[10] in his interesting paper on spontaneous gangrene describes and pictures obliterative endarteritis, which he believes to be of syphilitic origin, as a cause of this disease. The association of gangrene with the group of symptoms called "intermittent claudication," studied by Charcot, Goldflam, Erb, and others, and shown to be dependent on arterial disease, is well recognized. It is not to be doubted, therefore, that gangrene may be caused by endarteritis obliterans, nor is it difficult to understand why this should be so.

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[5] "On Local Asphyxia and Symmetrical Gangrene of the Extremities," by Maurice Raynaud. Translated by Thomas Barlow. London, 1888. The New Sydenham Society, vol. cxxi.

[6] *Transactions of the College of Physicians of Philadelphia*, 1898, 3. s., xx, p. 160.

[7] *Arch. f. klin. Chirurg.*, 1878, xxiii.

[8] *Deutsche Zeitschr. f. Chir.*, 1898, xlvii, p. 461.

Arterial thrombosis, with or without pre-existing arterial disease, is a demonstrated cause of senile gangrene, and may be the cause of the gangrene occurring occasionally as a complication or sequel of infectious diseases, particularly in influenza, typhoid and typhus fevers.[11]

2. *Can gangrene be caused by degenerative changes in nerves when the blood vessels are healthy?*

The idea that gangrene may be due to diseases of the nervous system alone without any vascular disease is not new. Raynaud[12] refers to the thesis by Zambaco[13] in which this view was expressed. The paper of Pitres and Vaillard[14] is often quoted in support of the possibility of gangrene resulting from degeneration of nerves. These writers reported two cases in which symmetrical gangrene of the feet occurred, and the arteries and veins were normal. The nerves of the lower limbs were much diseased below the knees, but not above. Those of the upper limbs were normal. Dehio[15] in criticising this paper states that the writers have not proven that gangrene may result from neuritis without vascular disease. Dehio, I think, is quite right in this criticism. The case does seem to show that endarteritis may be absent in gangrene, but the finding of nerve lesions and gangrene in the same limb does not prove that the latter is the result of the former. Both conditions may result from a common cause, or the gangrene may produce the degeneration of the nerves, as will be mentioned presently. In the report of a necropsy in a case of symmetrical gangrene Raynaud[16] says that the results obtained by himself were absolutely nil in so far as the circulatory system was concerned, so that without Pitres and Vaillard's case we have known for many years that gangrene may occur when the vessels are normal.

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[9] *Ztschr. f. klin. Med.*, 1896, xxxi, p. 130.

[10] Virchow's *Archiv*, 1898, clii, p. 26. Since the completion of this article C. Sternberg's paper (*Virchow's Archiv*, 1900, clxi, p. 199) has appeared with a full consideration of the relation of obliterating endarteritis to spontaneous gangrene.

[11] See Welch, Article "Thrombosis and Embolism" in Allbutt's System of Medicine, vol. vi, p. 178. London and New York, 1899.

[12] Loc. cit.

[13] Paris, 1857.

[14] *Arch. de phys. norm. et path.*, 1885, 3. s., v, p. 106.

[15] *Deutsche Zeitschr. f. Nervenheilk.*, 1893–4, iv, p. 1.

Dejerine and Leloir[17] in reporting two observations of gangrenous eschars of the skin, in which they found the nerves diseased, have collected most of the evidence existing at the date of their publication in favor of the occurrence of gangrene as the result of disease of the nervous system. The possibility that neuritis may produce gangrene must, I think, be admitted, although there is not agreement of opinion among authorities as to the interpretation of the experimental and clinical data adduced in support of this view.

3. *Does gangrene cause alterations of vessels and nerves?*

Lapinsky[18] has recently discussed this question quite fully and I cannot do better than to refer to his papers. The investigations of Hodson, Friedländer, Cornil and Ranvier, Ivanowski, Ziegler and others have shown that chronic inflammation has an injurious effect upon the vessels in the neighborhood and causes peri- and end-arteritis. Lapinsky noticed these changes of the vessels in some cases of his own in and near the gangrenous areas.

In reference to the nerves he says that the importance of local gangrene and suppuration in the production of changes in the nerves of the diseased limb has often been discussed without great weight being attributed to those conditions as etiological factors. He quotes a number of cases in which gangrene was found and was not believed to have caused degeneration of nerves, and he attributes no importance to the local gangrene in the production of the degeneration of the nerve stems in cases of his own. It is well known that ascending neuritis from a suppurating wound is of very rare occurrence.

Pitres and Vaillard allude to the fact that nerves passing to a gangrenous area do not necessarily show degeneration, and they say that this was recognized by Vulpian in 1866 and later by Dejerine and Leloir. However, it is probable that in some cases gangrene does cause alteration of nerves, possibly through alteration of the blood-vessels.

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[16] Loc. cit.

[17] *Arch. de phys. norm. et path.*, 1881, 2. s., viii, pp. 989 and 391.

[18] *Deutsche Zeitschr. f. Nervenheilk.*, xv, p. 364.

4. *Does degeneration of blood-vessels produce changes in the nerves of the same territory?*

In studying nerves for degenerative changes it is not sufficient to examine sections taken at a distance from the peripheral ends of the nerves. The increase in the degree of degeneration of nerve fibres towards the periphery was observed by Mannkopf in 1878 in a case of embolism of the popliteal and crural arteries.[19] The greater alteration of peripheral ends of nerves has also been seen by Hans Gudden[20] and other investigators. The importance of the recognition of this fact is seen, for example, in a case of spontaneous gangrene reported by C. Sternberg.[21] The sciatic nerve of the diseased limb did not contain degenerated nerve fibres but the vessels were much altered. I am unable to determine from the report of this case whether or not the peripheral ends of the nerves in the amputated limb were studied.

Schlesinger[22] says that the primary nature of the vascular disease and the secondary nature of the neuritis are not recognized by all, but he thinks that the vascular alteration occurs first. He reports a case in which pain in the feet and livid discoloration of the feet and hands were followed after some months by gangrene of the left foot. The left foot was amputated and the arteries and veins of the nerves within it were much thickened. The nerve fibres were normal in many bundles but in most they were more or less altered and the connective tissue of the nerves was proliferated. He thinks that without doubt the vascular degeneration occurred before the degeneration of the nerve fibres in this case, and he seems to have based this opinion chiefly on the clinical signs, and yet the disease began with pain in the feet as well as with livid discoloration.

When closure of an artery occurs the degeneration of the nerves may be only in the part below the thrombus, as seen in cases studied by Lapinsky. It is not necessary to quote many examples of this. We can accept without dispute the statement that a nerve speedily degenerates when its blood supply is abruptly cut off. Lapinsky says that in cases of acute ischæmia he found the changes of the nerve fibres more marked towards the distal ends where the effects of closure of the arteries were most felt.

The nerve changes are not so perceptible in chronic vascular disease, and according to Lapinsky they have been seen in only comparatively few cases. In some cases the changes of the nerve fibres were very slight and occurred only in certain areas; in other cases the nerve fibres were well preserved and the connective tissue about them was proliferated; in still other cases the nerves were perfectly normal. Lapinsky has collected the reports of a number of cases from the records bearing on this subject. He observed 8 cases of vascular disease; in 7 of these the arteries of one lower extremity were affected, and in one the arteries of both extremities were diseased, and gangrene developed in the part imperfectly nourished. The connective tissue of the nerves was increased in all the cases and this was especially true of the endoneurium.

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[19] Cited from Lapinsky.

[20] *Arch. f. Psychiatrie*, 1896, xxviii, p. 643.

[21] *Wiener klin. Wochenschr.*, 1895, viii, pp. 650, 687.

[22] *Neurologisches Centralblatt*, 1895, xiv, pp. 578, 634.

In the case reported in the present paper the ulnar nerve showed no degeneration as a result of the thrombosis of the ulnar artery.

Joffroy and Achard[23] seem to have been the first to describe neuritis of vascular origin. In a case of neuritis they found that the most pronounced lesions of the vessels were associated with the most pronounced lesions of the nerves, and from this they concluded that the degeneration of the nerves was due to the thickening and obliteration of their nourishing arteries. Neither this case nor the one published by Dutil and Lamy[24] establishes beyond question the vascular origin of neuritis although such an origin seems very probable. Dutil and Lamy say that in their case the parallelism existing between the vascular and nervous lesions justifies attributing the degeneration of the nerves to the thickening and obliteration of their nourishing arteries.

5. *Does degeneration of nerves cause alteration of the vessels in the same territory?*

Bervoets[25] claims to have demonstrated that cutting nerves causes thickening of arteries in the same territory, and he believes that he has demonstrated that neuritis is a cause of endarteritis. A. Fraenkel[25a] obtained similar experimental results, whereas C. Sternberg[25b] had only negative results. Czyhlarz and Helbing[25c] find an explanation of this discrepancy in their observation that changes in the vessels following experimental lesions of nerves occur only when ulcers result from the operation. Lapinsky[26] has collected from the records a large amount of evidence in support of the neuritic origin of endarteritis, and he concludes that these vascular disturbances may be of several varieties. In some cases the lumen is enlarged in the vessels of the territory in which the diseased nerves lie, and this part of the body becomes hyperæmic and its temperature is raised. The vessels may become broadened and lengthened and tortuous. In some cases the nutrition of the vascular walls is affected, as shown by local œdema and occasionally small hæmorrhages in the distribution of the diseased nerves. In some cases anatomical changes in the vessels have been found.

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[23] *Arch. de méd. expér.*, 1889, i, p. 229.

[24] *Arch. de méd. expér.*, 1893, v, p. 102.

[25] Over spontaan gangreen, etc., Nykerk, 1894.

[25a] *Wiener klin. Woch.*, 1896, ix, pp. 147, 170.

[25b] Loc. cit.

[25c] *Centralbl. f. allg. Path. u. path. Anat.*, 1897, viii, p. 849.

[26] *Zeitschr. f. klin. Med.*, 1899, xxxviii, p. 223.

Lapinsky refers to a number of clinical cases in which œdema or redness and increase of temperature followed injury or disease of nerves. This causes us to think of erythromelalgia, inasmuch as this redness and increase of temperature were found in later stages of neuritis as well as in the early. Alteration of nerves and vessels was very marked in a case of erythromelalgia reported by Dr. S. Weir Mitchell and myself.[27] Lapinsky refers to a number of cases in which changes in the walls of the vessels were believed to result from neuritis. He reports two cases in which disease of the walls of the vessels developed in the distribution of diseased nerves. He believes that the disease of the nerves causes a loss of tonicity and elasticity in the walls of the vessels and a disturbance in the nutrition of the vessels; the enlargement of the lumen, the increased intravascular pressure and the slowing of the blood current lead to further changes.

I have referred elsewhere[28] to the views of Thoma. Thoma has shown that when the lumen becomes too great in proportion to the amount of blood flowing through it, as for example after amputation, a compensatory connective tissue thickening of the intima occurs and the proper relations are restored. He has shown that neuritis produces a similar change in the vessels.[29] He studied the soft tissues taken from both temples in a case of left supraorbital neuralgia. More or less hyperæmia occurred in the painful area at the time of the attack. He found that the arteriosclerosis in the area of the supraorbital neuralgia was considerably greater than in the corresponding area on the other side. Thoma had acquired so extensive a knowledge of the vascular system that he was able to name most of the large arteries when transverse microscopical sections of them were shown to him. It seems that the vasomotor change caused by the pain in Thoma's case led to this thickening of the intima.

[27] *Amer. Jour. Med. Sciences*, Jan., 1899, cxvii, p. 1.

[28] Ibid.

[29] *Deutsches Arch. f. klin. Med.*, 1888, xliii, p. 409.

More recently this subject has been again studied by Lapinsky.[30] Although the evidence, especially on the experimental side, is conflicting, there is support for the view that degeneration of nerves may cause degeneration of vessels.

From the preceding statements and review of the evidence relating to the association and correlation of arteritis, neuritis and gangrene it may, I think, be stated:

1. Gangrene may be caused by endarteritis obliterans.
2. Alteration of nerves alone without alteration of the vessels is believed by some to be a cause of gangrene. We need probably more evidence before this conclusion can be definitely accepted.
3. Gangrene may cause degeneration of the vessels, especially of the portions near the gangrenous area.
4. Gangrene is less liable to cause degeneration of nerves except of the portions within or near the gangrenous areas.
5. Sudden closure of blood-vessels causes degeneration of the nerves nourished by these vessels, unless an adequate collateral circulation is promptly established. If the vascular disease is of a chronic type the nerves may escape, at least for a time, but do not always do so, the result doubtless depending upon circulatory conditions which vary in different cases.
6. Degeneration of nerves is a possible, but not thoroughly demonstrated, cause of degeneration of the blood-vessels.

I have noticed in this and other cases of arterio-sclerosis a multiplication of the elastic membrane. This is probably a new formation. It has been regarded by some as merely a separation of the layers of the previously existing elastic membrane, but this explanation is not satisfactory for all cases. In order to furnish so much new elastic tissue the old must have become very much thickened. I have found an elastic membrane in the organized thrombus of the case A. A., and the thrombus was here separated by a clear space from the proliferated intima. It probably represents here newly-formed tissue. Similar views are held by Dmitrijeff[31] and others.

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[30] Lapinsky, *Arch. de méd. expér.*, 1899, xi, p. 109.

[31] *Ziegler's Beiträge*, 1897, xxii, p. 207.

The case of A. A. was not a typical one of Raynaud's disease but it bore certain resemblances to it as Dr. Sinkler pointed out. Local syncope or local asphyxia is not mentioned in the history. The affection was of the distal parts of both upper extremities, in which papulovesicles were important features. Dr. Sinkler describes the sloughing process as first a discoloration of the skin, involving perhaps one-half the surface of the finger; this portion of the finger rapidly became black, then dry, and the slough was thrown off leaving a granulating surface. This account is not unlike that of a case of Raynaud's disease. Monro,[32] in his excellent monograph on Raynaud's disease, says that in less than two per cent of the cases of this disease gangrene alone is mentioned, and a careful perusal of these cases makes it almost certain that there was a stage of asphyxia. In the same proportion of cases, syncope and gangrene alone are mentioned, but in the majority of these asphyxia also was probable. This case A. A. could be considered at most only as an atypical one of Raynaud's disease, but it may have a similar etiology.

There is a class of trophic diseases having certain resemblances to one another but still with distinctive features. Erb[33] compares Raynaud's disease with intermittent claudication. The two disorders resemble one another in the paræsthesia and pain, in the vasomotor disturbances, in the cutaneous gangrene of the fingers and toes, and in the occasional mutilation. In Raynaud's disease neurasthenia, even psychopathies, may occur; the fingers are chiefly implicated; the gangrene is usually limited to the superficial layers of the skin; the symptoms are paroxysmal but not so intermittent as in intermittent claudication and do not depend directly on the use of the limbs. In Raynaud's disease marked changes in the vessels (arteriosclerosis, absence of pulse) and severe gangrene have not been observed. After making these distinctions, Erb refers to Dehio's findings of endarteritis and phlebitis in a case of Raynaud's disease, and says that after all there may be a closer resemblance between Raynaud's disease and intermittent claudication than has been supposed.

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[32] T. K. Monro, Raynaud's Disease. 1899.

[33] *Deutsche Zeitschr. f. Nervenheilk.*, 1898, xiii, p. 1.

Angiosclerosis, according to Erb, is manifested clinically in a variety of forms. Simple or obliterating arteriosclerosis without nervous symptoms causes senile gangrene or simple spontaneous gangrene; the combination of obliterating arteritis with symptoms of vasomotor irritation and of sensory and motor disturbance causes the intermittent lameness; the combination of symptoms of vasomotor paralysis (possibly of irritation of the vasodilators) with sensory irritation and obliterating arteritis is possibly the cause of erythromelalgia; the combination of obliterating arteritis with vasomotor and trophic and nervous symptoms may be the cause of Raynaud's disease; the combination of arteritis with intense degeneration and inflammation of the nerves causes the angiosclerotic neuritis of Joffroy and Achard, Dutil and Lamy, and Schlesinger; the vasomotor and sensory irritation without the endarteritis causes acroparæsthesia. It is to be noted that in these diseases a functional disturbance in addition to an organic one is common, and in reading the clinical report of the case A. A. as given by Dr. Duhring and Dr. Sinkler I am impressed by the fact that the disturbance was certainly in large part functional.

The interpretation of the lesions found in the case A. A. is difficult. The woman had stigmata of hysteria and probably had Graves' disease. Destruction of nerves near the seat of spontaneous amputation is nothing more than one might expect as a result of the amputation and suppuration. This degeneration decreased upward quite rapidly, and 6 cm. above the styloid process of the radius was slight in the radial nerve except by the Marchi method and was not very evident in the ulnar or median nerve at parts only a short distance from the seat of spontaneous amputation. The vascular disease seems hardly sufficient to explain the loss of the fingers. The ulnar artery from the amputated limb was nearly closed at one part by an organized thrombus, but this had not caused degeneration of the accompanying ulnar nerve, and it is hardly reasonable to suppose that it had caused such serious changes as the loss of the fingers. The alteration of the radial artery was certainly insufficient to explain the symptoms. The right brachial plexus was normal and there was no evidence here of ascending neuritis. The alteration of the left brachial plexus as seen by the Marchi method is difficult to explain. The appearances were those of recent degeneration. Shall we believe that trophic lesions would have reappeared in the left upper limb if the patient had lived longer, or shall we believe that the findings were artefacts? The left radial nerve was as much altered as the right radial 6 cm. above the styloid process of the radius. This alteration may have been due to the serious lesions that had formerly existed in the left upper limb. Dr. Sinkler regarded the case as a trophoneurosis dependent upon an hysterical diathesis. There is much to be said in favor of this opinion, but there was nevertheless neuritis of high degree in the periphery of the right upper limb, moderate degeneration of nerves several centimetres above the wrist of the same limb, and some vascular change in the amputated part; and the radial of the left upper limb was diseased. The question as to whether these lesions were primary or secondary I do not think can be positively determined. I have attempted to show that they might have been either. At all events the condition in A. A. was not the result of any distinct lesion in the central nervous system. Functional disturbances in the circulation of the peripheral ends of the limbs, in connection with the organic changes, probably increased the peculiar lesions in the case A. A. Her relapses seemed to depend to some extent on functional disorder.

Dehio[34] examined fingers that had been amputated on account of Raynaud's disease and found in these endarteritis, endophlebitis and degenerated nerves, but he only had about 1 cm. of normal tissue above the gangrenous area for his investigation. He, too, was uncertain whether the vascular sclerosis preceded the gangrene or vice versa.

The microscopical examination in the case I report is valuable on account of the extreme rarity of a case of this character with necropsy. It would be most unscientific, however, to be too positive in the interpretation of the lesions, although these were of a definite character, as I have already shown that there is at present considerable difference of opinion concerning the explanation of similar or identical lesions in cases of gangrene.

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[34] *Deutsche Zeitschr. f. Nervenheilk.*, 1893–4, iv, p. 1.

Dr. Duhring in his two papers in which he reports clinically the case A. A. refers to several similar cases in the literature. A brief review of some of these may be of interest and of assistance in judging of the etiological value of the findings in the case A. A.

Doutrelepont's[35] case was one of multiple gangrene of the skin over a large portion of the body, associated with vesicles and following the penetration of a needle beneath the left thumb in a hysterical woman. The spinal cord and nerves examined in this case were found to be normal, and the results of the necropsy did not in any way explain the disease.

The case reported by Kopp[36] resembles that reported by Doutrelepont. In Kopp's case the lesions were observed on the left breast, left forearm and left thigh. The neurotic nature of the affection Kopp believed was shown by the unilaterality, the acute development of the lesions in groups, the typical course, and the accompanying neuralgia. An ulcerating keloid on the left hand which developed in the scar of a burn, he thought might have caused ascending neuritis and implication of the spinal cord. Kopp describes the case as one of multiple neurotic cutaneous gangrene.

Galton's[37] patient was a girl of seventeen who had suffered from fits of an epileptic nature, brought on by a fright at school. Patches of redness followed by blebs appeared on the left wrist, hand and arm shortly after she had chopped off the distal phalanges of the index and ring fingers and cut through the middle phalanx of the middle finger. The eruption was peculiar from the rapid way in which it spread. Sometimes within a quarter of an hour the whole hand and arm would be covered with large blebs which would burst and discharge. The circulation seemed very feeble. At one time a crop of vesicles appeared on the left leg. Galton attributed the lesions to a reflex irritation.

Kaposi's[38] patient was a girl of twenty-two years, who had injured her right middle finger by a nail. The part was bound in iodoform. A few days later vesicles appeared on the dorsal surface of this finger and extended and affected the back of the hand and forearm. These vesicles were accompanied by a sensation of burning in the part. Other cutaneous surfaces of the body were attacked. Kaposi did not believe a neuritis existed but thought that an ascending irritation was present and caused redness, exudation and vesicles, and that this irritation extended to the spinal cord. He thinks his case resembled Doutrelepont's, and that it was an expression of hysterical irritability of the vasomotor system, analogous to cases of herpes zoster gangrænosus and of zoster gangrænosus hystericus. No gangrene was observed in Kaposi's case. He calls his case "pemphigus neuroticus hystericus."

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[35] *Vierteljahresschrift f. Dermat. u. Syphilis*, 1886, xiii, p. 179, and *Arch. f. Dermat. u. Syphilis*, 1890, xxii, p. 385.

[36] *Münch. med. Wochenschr.*, 1886, p. 665.

[37] *British Med. Journal*, 1891, i, p. 1282.

[38] *Wiener klin. Wochenschr.*, 1890, p. 425.

Bayet[39] describes a condition known as disseminated cutaneous gangrene. He speaks of it as a very rare affection. Some of the cases have been described, he says, as gangrenous zona, others as pemphigus neuroticus, and others as gangrenous urticaria. The causes of this confusion are the rarity of the affection and the predominance of certain symptoms in different cases; but common to all are the dependence of the lesions on disturbances of innervation and the local evidences of hysteria. Bayet's case is as follows:

A hysterical male, nineteen years of age, burned himself superficially on the anterior surface of the left forearm a little above the wrist. The wound healed at the end of twelve days. Two days after the accident plaques covered with a dry crust appeared on the external surface of the thumb. This crust did not last very long and left a superficial ulcer requiring two months to cicatrize. Within a short time twenty-one ulcers of different sizes, some as large as a franc, appeared on the left forearm. All these ulcers were found on portions of the skin which had not been in contact with the sulphuric acid. These lesions were found later on the hand. Deeply pigmented areas represented the former site of ulcers, and in some of these areas bullæ, containing a sero-sanguineous fluid, appeared. The skin between these lesions seemed to be normal. The case was believed by Bayet to be a multiple gangrene of the skin dependent upon hysteria. He was able to produce a characteristic lesion by suggestion.

Janovsky and Mourek[40] in a study of multiple cutaneous gangrene report two cases in which vesicles were observed but no necropsy was obtained. They give references to several cases of cutaneous gangrene. Whether these cases of cutaneous gangrene should be classed with such a case as that of A. A. in whom the lesions were chiefly of the character of vesicles is questionable. The etiology in all is obscure.

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[39] *Annales de dermat. et de syphiligraphie*, 1894, v, p. 501.

[40] *Arch. f. Dermat u. Syphilis*, 1896, xxxv, p. 559.

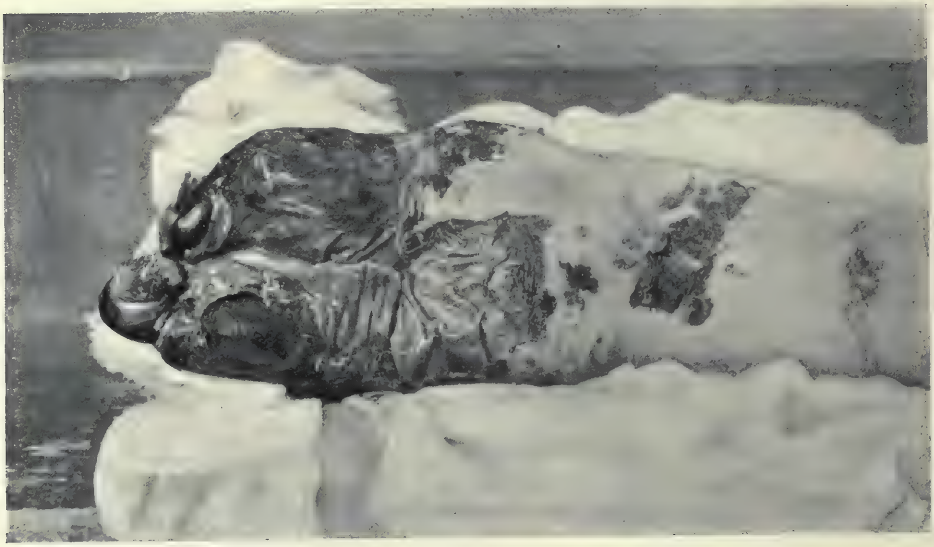

FIG 1.

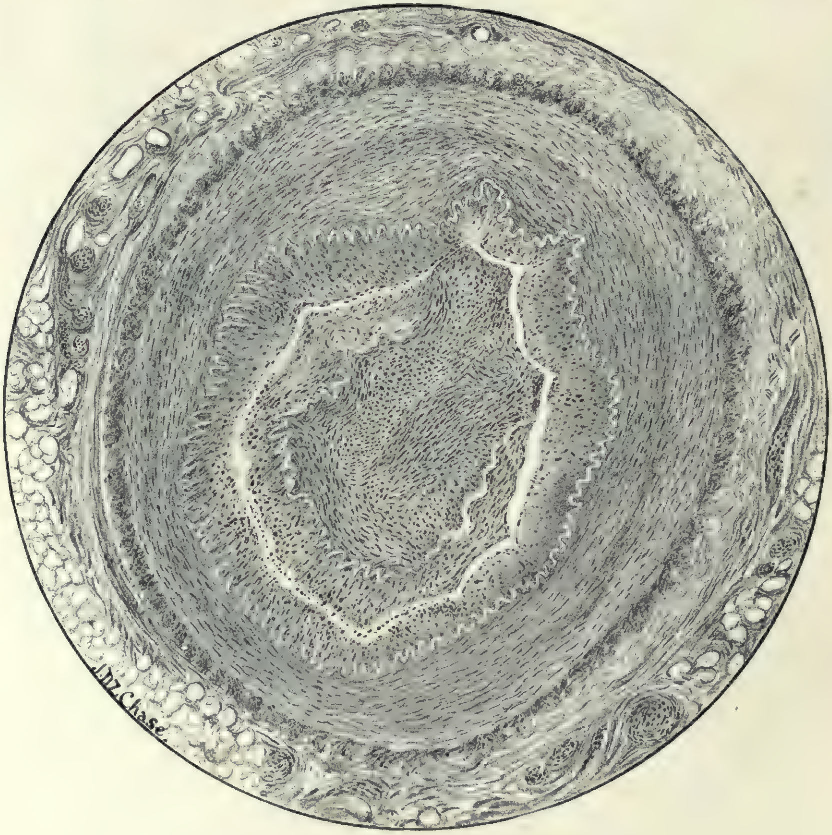

FIG. 2.

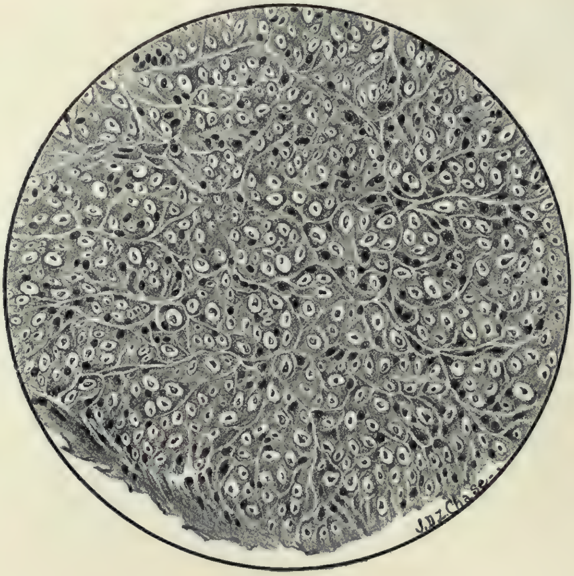

FIG. 3.

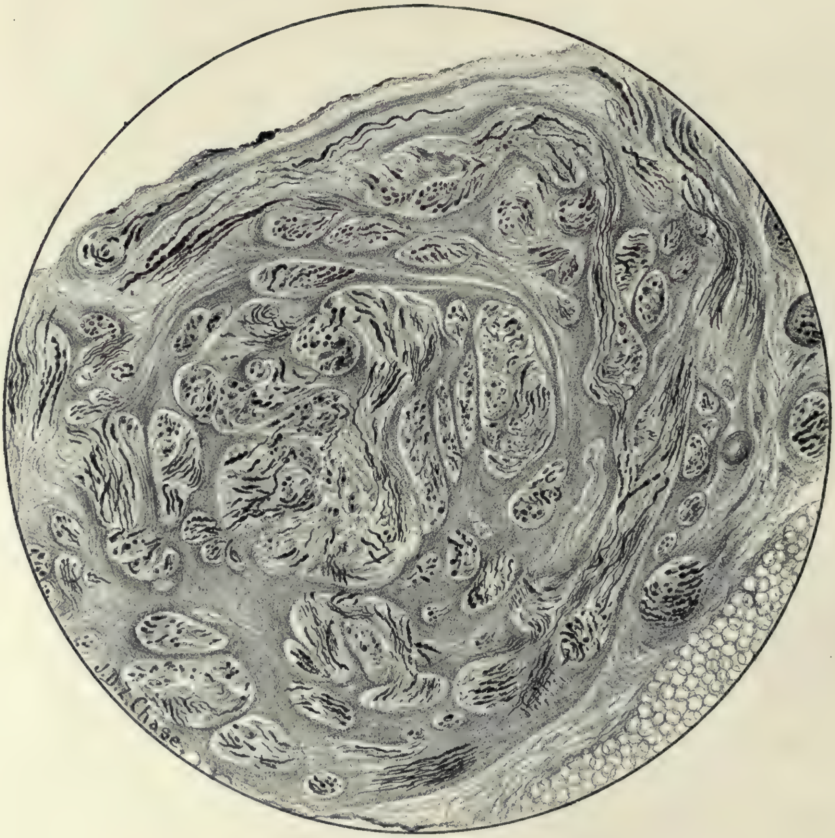

FIG. 4.

DESCRIPTION OF PLATES IV AND V.

PLATE IV.

Fig. 1.—Photograph of the amputated part of the right forearm and hand, palmar aspect.

Fig. 2.—An organized thrombus in the right ulnar artery from the amputated part of the limb.

PLATE V.

Fig. 3.—Section of the radial nerve from the right forearm taken 6 ctm. above the styloid process of the radius. The nerve fibres are diminished in number and the endoneurium is proliferated. The degeneration is much less than in the more peripheral portion of the nerve (see Fig. 4).

Fig. 4.—The radial nerve from the right upper limb in its terminal portion. The degeneration of nerve fibres and the overgrowth of connective tissue are extreme.

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RENAUT'S BODIES IN A CASE OF VESICULOBULLOUS DERMATITIS AND GANGRENE.[1]

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[From the William Pepper Clinical Laboratory, Phœbe A. Hearst Foundation.]

In examining the left brachial plexus in a peculiar case of vesiculobullous dermatitis and gangrene, described more fully in my pathological report in the *Journal of Experimental Medicine*, Vol. V, No. 1, I found structures within some of the nerve bundles that are doubtless the formations described by Renaut[2] in 1881, and later by other writers. They are sometimes called Renaut's bodies (Körperchen), although Renaut does not seem to have been the first to men-

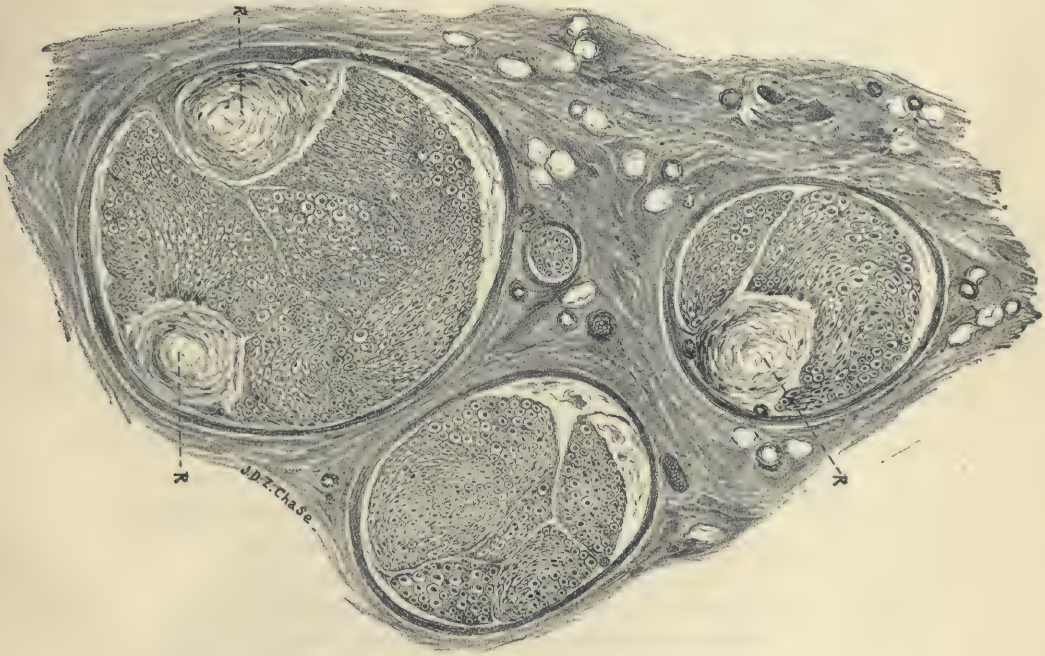

FIG. 1.—Transverse section of nerve bundles in brachial plexus.
R. R. R.—Renaut's bodies in transverse section.

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[1] Read before the University of Pennsylvania Medical Society, October 19, 1900.

[2] Renaut, *Archives de physiologie normale et pathologique*, 1881.

tion them. They are not so well known as is desirable, and there is some danger therefore that they may be regarded as a new and unrecognized form of degeneration of nerves. A description of them has recently been given by F. Pick[1] and also by Nawratzki.[2] I have no theory to offer in regard to their function, but there seems to me to be little evidence that they are intended for the protection of nerve fibres, as has been held by some observers. They have been seen in the nerves of man and the lower animals, and in both normal and pathological conditions, by quite a number of investigators, and yet there are probably many pathologists who are not familiar with them. The central part of one of the Renaut's bodies examined by F. Pick appeared to contain a nerve fibre. Pick does not regard them as pathological structures, but he, like every one else who has studied them, is unable to give any positive statement regarding their function. Other investigators are in doubt whether they should be regarded as pathological formations or not, and the mystery surrounding them is greater than that surrounding the muscle spindles, as the latter are now believed by many observers to be concerned with the muscular sense.

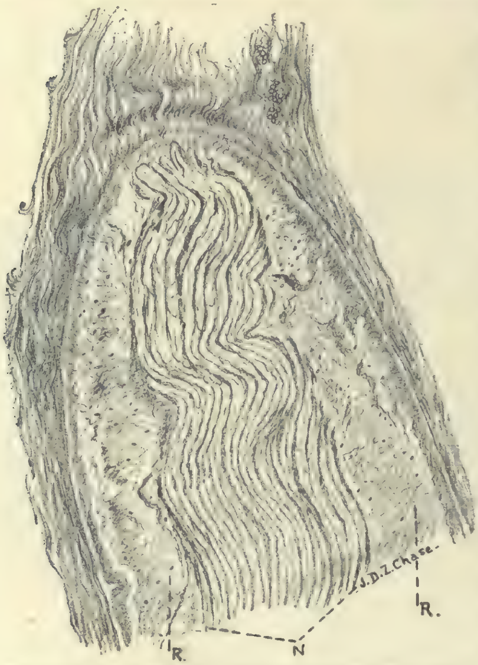

FIG. 2.—R. R. Longitudinal Section of Renaut's bodies. N. Longitudinal section of nerve bundle.

In the case studied by me the Renaut's bodies in one of the nerves of the left brachial plexus are quite numerous, and two are found in one of the nerve bundles. They are formed of delicate wavy bands of connective tissue arranged concentrically in a transverse section of a nerve, and chiefly longitudinally, though in some places transversely, in a longitudinal section. They contain a few oval nuclei, also arranged concentrically in a transverse section, and a nucleus is usually within one of the bands of wavy connective tissue. A central homogeneous mass is not very distinct in my preparations. In longitudinal sections of a nerve the Renaut's bodies are much longer than broad, and are sometimes spindle-shaped. I have not been able to observe anything resembling a nerve or vessel in the centre of any one of them. They are usually at the periphery of the nerve bundle, but may be in the centre, and while generally round in transverse section, are not always so. They are always sharply separated from the surrounding nerve fibres, and this is one indication that they probably are not degenerated tissue.

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[1] F. Pick, *Deutsche Zeitschrift für Nervenheilkunde*, Vol. XVII, Nos. 1 and 2, 1900.
[2] Nawratzki, idem.

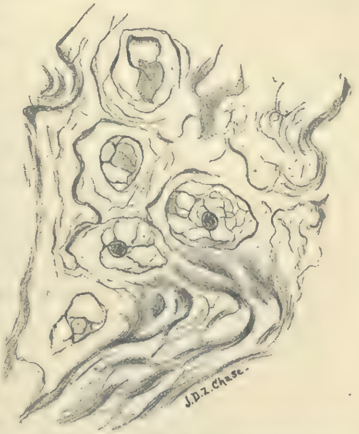

FIG. 3.—Multilocular cells found in the Renaut's bodies.

I have found the peculiar cells discovered by Langhans and named by him "ein und mehrkammerige Blasenzellen" (one-and-more-chambered bladder cells), which might be translated as multilocular cells. According to the description given by J. Kopp and T. Langhans, these cells are large and of various forms, and contain many dividing septa and one to three, seldom more, nuclei near together. These nuclei are large and oval, and contain one or more nucleoli, and are surrounded by a zone of protoplasm.[1]

These extraordinary cells in my specimens are very irregular in shape, and the cell-body is unstained except in the dividing septa. Such a cell by changing the focus appears to be composed of numerous compartments, wherefore the name given by Langhans.

The brachial plexus seems to be a favorite place to search for the Renaut's bodies. It was here Preisz found them, and Trzebinsky examined chiefly this plexus. Preisz thinks there is a resemblance between these bodies and the muscle spindles, and calls the former "Nervenknospen" and the latter "Muskelknospen." Loose, wavy connective tissue forms a large part of both the Renaut's bodies and

[1] J. Kopp, *Virchow's Archiv*, 128, 1892, p. 290; T. Langhans, idem, p. 318.

the muscle spindles, but in the former muscle fibres are absent. The bladder cells (Blasenzellen) were not so large and not so numerous in Preisz's case as in those described by Langhans and Kopp, and they were absent in some of the Renaut's bodies examined by Trzebinsky (cited by Preisz),[1] but were quite numerous in my preparations.

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[1] Preisz, *Deutsche Zeitschrift für Nervenheilkunde*, Vol. VI, 1895, p. 101.

A CASE WITH THE SYMPTOMS OF CEREBRO-SPINAL MENINGITIS, WITH INTENSE AND GENERAL ALTERATION OF THE NERVE CELL-BODIES, BUT WITH LITTLE EVIDENCE OF INFLAMMATION.[1]

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The following case is interesting because symptoms of meningitis existed for six days and yet lesions sufficient to explain these symptoms were not found at the necropsy. The intense and general alteration of the nerve cell-bodies suggests some remarks relative to the similar lesions observed in amaurotic family idiocy.

According to the records in the case-books of the Pennsylvania Training School for Feeble-Minded Children, F. S. M. was born July 11, 1892, and was admitted to the Training School, March 19, 1900. The parents of the child are living and in good health. The father, a teamster, was thirty-two years of age, and the mother twenty-six at the birth of this their fifth child. There is no history of intemperance in parents or grandparents. F. was born at full term, but in difficult labor, lasting three days. One brother and one sister of the boy are living, and are healthy, mentally and physically. F. was of feeble mental development; he did not know the alphabet, did not talk and could not dress himself properly. His sight and hearing were good. His gait was spastic. He was of small size, and had scoliosis. Sensation was normal so far as could be determined. He did not have convulsions.

The following notes were made by Dr. W. G. Shallcross, the resident physician:

"April 1, 1900. I was called early this morning to see F. and found him in considerable pain, which he could not locate. The skin was hot and dry, pulse was rapid and he had diarrhea and vomiting. In the afternoon he was not so restless. The bowels had moved once. The heart's action was rapid and the second sound was accentuated, but there was no murmur.

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[1] From the Wm. Pepper Clinical Laboratory, Phœbe A. Hearst Foundation.

Read before the Philadelphia Neurological Society, November 26, 1900.

The condition of the lungs was normal. The liver and spleen were not enlarged. Urine was passed involuntarily.

"April 2. F. was not so well to-day. He was more restless, but it was impossible to determine the location of the pain. The abdominal muscles were rigid, but showed no tenderness on pressure. He retained food.

"April 3. He was very restless and the skin was hypersensitive. The pupils were equal and seemed to react sluggishly. He had some photophobia. The abdominal muscles were rigid and the legs were drawn up on the abdomen as if the boy were in pain.

"April 4. Photophobia was quite pronounced. The pupils were about 3 mm., equal, and did not react to light. The neck was somewhat rigid and the head was retracted slightly. The muscles of all the extremities were stiff and the hands were thrown about wildly when the patient was disturbed. Hyperesthesia was very pronounced. The thighs were frequently flexed upon the abdomen.

"April 5. F. had a very restless night and was delirious at times. An erythema was noticed this morning about the right knee and calf. No albumin was found in the urine.

"April 6. Coma is developing and the patient is more quiet. The rash is spreading. He could not take food and was nourished by the rectum. Death occurred at 9.30 P. M."

A diagnosis of cerebro-spinal meningitis was made by Dr. Shallcross.

The necropsical notes are as follows: Cadaveric rigidity was present. Numerous small, dark-reddish spots of various sizes and shapes were seen on the anterior surfaces of the thighs, on the outer and inner parts of the legs below the knees, and on the anterior surfaces of the upper limbs.

Brain: The scalp was very adhesive to the skull. The cerebral dura was adherent to the calvarium at the coronal and sagittal sutures. A large amount of cerebro-spinal fluid tinged with blood escaped when the calvarium was removed. The brain was edematous. The superior longitudinal sinus contained a few soft clots. The dura was slightly adherent to the pia in small areas at the anterior part of the right frontal lobe and at the right temporal convolutions. No distinct evidences of inflammation could be detected with the naked eye. The pia about the optic chiasm and covering the interpeduncular space was somewhat opaque in patches, but hardly more than is seen in many normal brains. No miliary tubercles could be found.

Heart was small, normal in position, and the pericardial fluid was not excessive. Right auricle and pulmonary artery contained chicken-fat clots. Tricuspid valve admitted two fingers and was normal. Mitral valve admitted the middle finger easily. Left auricle did not contain any clot. A chicken-fat clot was found in the right ventricle. The mitral and aortic valves appeared to be thickened. The cardiac muscle was a little pale.

Lungs: Right lung was somewhat edematous, but crepitated, and did not contain any areas of consolidation. The left lung was in the same condition as the right. There were no pleural adhesions on the left side, but some old adhesions were found on the right side. The diaphragm extended to the fourth rib on each side.

Liver was of good size and smooth, and extended to the border of the last rib. Reddish spots were seen on the upper surface, especially on the left lobe. The tissue was somewhat yellow on section and numerous small reddish areas like hemorrhages were found. The gall bladder was full.

Spleen was of normal size and of dark slate color. A small supernumerary spleen was found.

Pancreas appeared to be normal.

Suprarenals appeared to be normal.

L. Kidney: Capsule stripped easily and the surface of the kidney was smooth. No cysts were found. The tissue was pale on section; the cortex was somewhat yellowish. The pyramids were fairly distinct. The right kidney was in the same condition as the left.

Stomach was congested and small hemorrhages were found on its inner surface.

Bladder was normal and filled with urine.

Weight of brain, 1,040 grm.; heart, 80 grm.; left lung, 165 grm.; right lung, 175 grm.; left kidney, 75 grm.; right kidney, 65 grm.; liver, 810 grm.; spleen, 90 grm.

It is not surprising that this case was diagnosticated as one of cerebro-spinal meningitis, on account of the acute onset of the disease with fever of 102 degrees F., diarrhea and vomiting; the pain, the rigidity of the abdominal muscles, the hyperesthesia of the skin, the photophobia, the stiffness of the neck, etc. The microscopical examination of the nervous tissues, however, showed little evidence of inflammation. The nerve cell-bodies throughout the central nervous system were greatly altered and this alteration was not confined to the cells with motor function. It was seen in the cell-bodies of the posterior and anterior horns of the spinal cord, in the nuclei of the cranial nerves, in the sensory, as well as the motor, nucleus of the fifth nerve; in the cells of Purkinje and in the parietal lobule, where especially the cells of Betz were altered. The cell-body was swollen and rounded; many of the dendritic processes had disappeared; the chromophilic elements were not to be seen, except in one portion of the cell-body, where they surrounded the nucleus, and even here were more or less disintegrated, and the nucleus had moved to the periphery of the cell-body. This description applies to most of the nerve cell-bodies of the central nervous system. The appearance presented by the cell-bodies of the anterior horns

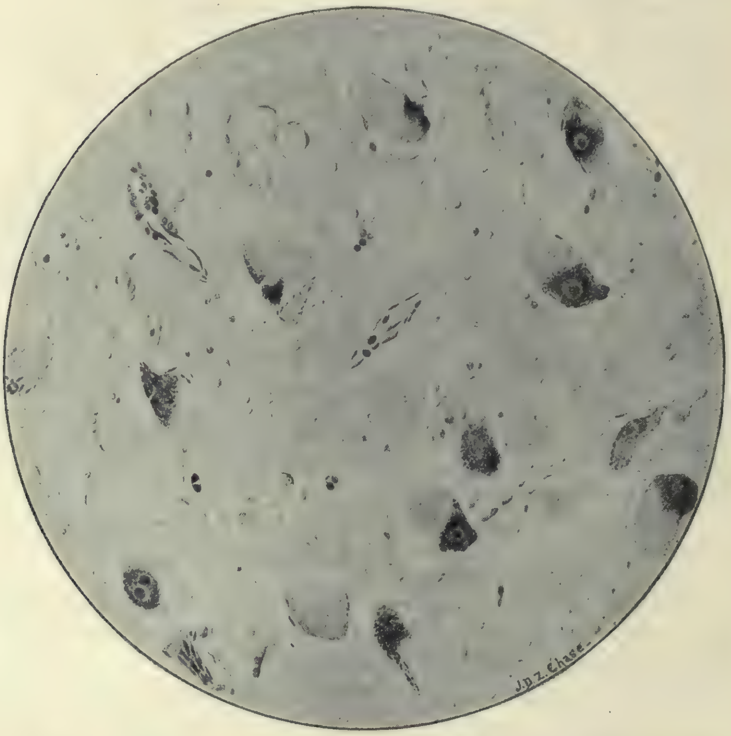

Fig. I. Cell-bodies of the anterior horns in the lumbar region. They are represented as they appear in *one* field of the microscope, in order to show the intense alteration of all the cell-bodies.

was most extraordinary, as all the cell-bodies had undergone this peculiar alteration (Figs. I. and II.).

The lesions of meningitis were not found. A very slight round-cell infiltration was observed in some parts of the pia (Fig. III.) and about some of the intramedullary blood vessels, but the small vessels of the pia and anterior and posterior roots were much distended with blood. Numerous small bacilli were found within the nervous tissues.

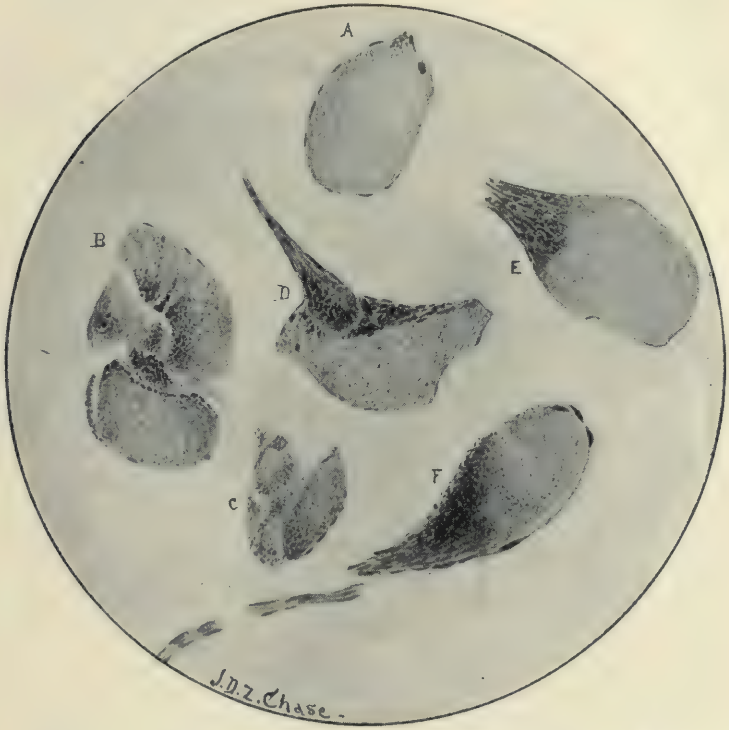

Fig. II. Selected cell-bodies from the anterior horns of the lumbar region, with the exception of cell-body E, which is from the paracentral lobule. Cell-body A shows complete chromatolysis. The cell-bodies B and C are divided into several parts. In D, E and F the chromophilic elements are seen in only one part of the cell-body, and the nucleus is not distinct.

In a case of amaurotic family idiocy Hirsch[2] observed a very extraordinary change in the nerve cell-bodies of the central nervous system. All the cell-bodies of the anterior and posterior horns were greatly enlarged and round. The nucleus was at the periphery of the cell-body and was sharply defined, and contained a nucleolus staining deeply. The nucleus was surrounded by a dark zone gradually shading off into a more or less colorless area. The dark zone contained broken-down chromophilic elements and occasionally a few normal ones. The light area of the cell-body was made up of a very fine network. Some of the cell-bodies were vacuolated. The dendrites and axone of the cell were very few, and many of the processes seemed to be broken off. The pictures of these cell-bodies represent them as swollen,

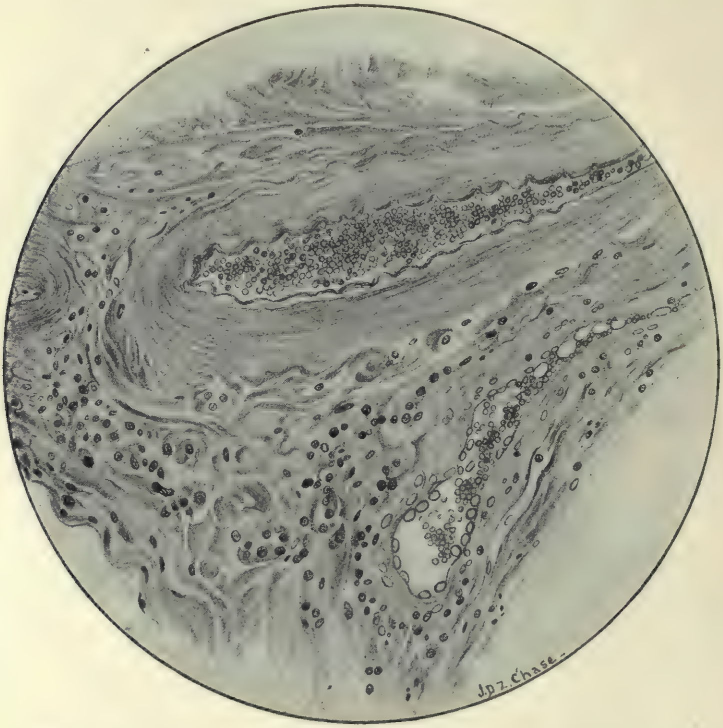

Fig. III. The pia of the anterior fissure of the spinal cord, showing a slight round-cell infiltration. Nowhere is the cellular infiltration more intense than that represented in the drawing.

almost round masses. The same alteration was found in all the cell-bodies of the central nervous system, although the cell-bodies of the cerebellum were not much affected. Hirsch found degeneration of the pyramidal tracts. When he examined some of the preparations from a case of amaurotic family idiocy reported previously by Sachs, he found in these a similar change of the nerve cell-bodies, although the material had been hardened in Müller's fluid. Hirsch refers to no cases that were not of amaurotic family idiocy, in which a similar change of all the nerve cell-bodies was found, and he states that no disease is known in which simultaneously all the nerve cell-bodies of the entire nervous system become affected. The condition of the nerve cell-bodies in his case, he thought, corresponded in every respect to that found after experimental poisoning, and amaurotic family idiocy is therefore an acquired disease and is produced by some poison, possibly by a toxic condition of the mother's milk.

Sachs[2] argued in the discussion of this paper that a disease so widespread as amaurotic family idiocy, which begins always at the same period of life, and attacks several members of the same family and leaves others exempt, could not be due to any toxic influence that is known to us. From this we may conclude that Sachs either did not regard the alteration of the nerve cell-bodies as of toxic origin, or else he thought that this cellular degeneration did not explain the disease. Hirsch, in closing the discussion on amaurotic family idiocy, remarked that the toxic origin of the disease was an open question. He knew of no other inherited family affection where all the nerve cell-bodies, and nothing but the nerve cell-bodies, became diseased, and the condition, so far as he knew, had no analogy in pathology.

I have seen this same general alteration of the nerve cell-bodies of the central nervous system in two cases, and neither was a case of amaurotic family idiocy. One was a case of internal hemorrhagic pachymeningitis in an idiotic child aged nine years, and the microscopical report was published by me[3] in collaboration with Dr. D. J. McCarthy. Even by the carmine stain the alteration of the cell-bodies in preparations hardened in Müller's fluid was most striking. The pyramidal tracts were not degenerated, which is interesting in view of the intense alteration of the motor cell-bodies. In Hirsch's case these tracts were degenerated.

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[2] Hirsch, Sachs. THE JOURNAL OF NERVOUS AND MENTAL DISEASE, 1898, No. 7, pp. 538, 555.

[3] Spiller and McCarthy. THE JOURNAL OF NERVOUS AND MENTAL DISEASE, 1899, No. 11, p. 677.

The second case in which I have observed this intense and general alteration of the nerve cell-bodies of the central nervous system is the one with symptoms of cerebro-spinal meningitis reported in this paper. It is noteworthy that the cellular alteration in these two cases was in children of feeble mental development, as in the cases of amaurotic family idiocy, and such cellular alteration is therefore not confined to amaurotic family idiocy.

A theory of a toxic condition in the second case could be well supported by the clinical history, but not so well in the case of internal hemorrhagic pachymeningitis, although even in this it could not be absolutely rejected. The alteration of the nerve cell-bodies throughout the central nervous system is extraordinary, and yet in the two cases in which I have observed it secondary degeneration has not occurred. I am not aware that such an intense and widespread alteration of the cell-bodies of the central nervous system has been observed by other investigators in cases of disease of the human nervous system.

The symptoms of cerebro-spinal meningitis sometimes occur in typhoid fever and other infectious diseases without alteration of the meninges, and to this form of pseudo-meningitis the name of *meningisme* has been given by Dupré, and Schultze has spoken of "meningitis without meningitis." It is not impossible that in some of these cases an alteration of the nerve cell-bodies similar to that in my case occurs. A paper bearing on this subject has recently been published by Finkelstein.[4] He says a few cases of longer or shorter duration have been observed in which the symptoms were indicative of meningitis and were fever, convulsions, rigidity of the neck, hyperesthesia and opisthotonos, and yet at the necropsy only slight edema and softening of the brain and a small excess of ventricular cerebro-spinal fluid were found. He did not regard this condition as a true meningitis serosa, but as inflammatory cerebral edema, because cellular infiltration of the meninges has been observed in a few cases.

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[4] Finkelstein. Monatsschrift für Psychiatrie und Neurologie, Vol. 8, No. 4.

Finkelstein shares the opinion of Seitz that some toxic substance in the crebro-spinal fluid is the cause of this slight inflammatory edema, and that pathogenic bacteria in the cerebro-spinal fluid may cause severe cerebral symptoms without causing a distinct meningitis. He points out that in some cases meningitis serosa has been found to be due to the presence of bacteria. It seems that meningitis serosa cannot be sharply distinguished from the inflammatory cerebral edema.

It is important to remember that pronounced symptoms of meningitis may be present with very slight alteration of the meninges, and that even purulent meningitis may exist without any symptoms. In my case the brain was edematous, and on microscopical examination, very slight cellular infiltration could be found in the pia, so slight as to be questionable, but the nerve cell-bodies throughout the central nervous system were intensely altered, and yet there is doubt concerning the relation of this alteration of the nerve cell-bodies to the symptoms of meningitis.

Numerous bacteria were found within the nervous tissue of my case, reported in this paper, and while Dr. S. S. Kneass, to whom I showed a section, recognized them as short bacilli, he was unwilling to give them a name. The symptoms of the case and a slight perivascular round-cell infiltration would indicate that these bacilli were probably within the tissues before death, and yet the recent paper by Zappert[5] on the presence of micro-organisms within the spinal cord shows how difficult it is to decide whether a bacterial invasion has occurred before or after death. The intense alteration of the nerve cell-bodies in my case may possibly have been the result of a toxin, but it has not been demonstrated that this is the correct view.

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[5] Zappert. Obersteiner's "Arbeiten," Vol. 7.

Extracted from The American Journal of the Medical Sciences, December, 1900.

A CASE OF MALARIA PRESENTING THE SYMPTOMS OF DISSEMINATED SCLEROSIS, WITH NECROPSY.[1]

By William G. Spiller, M.D.,
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(From the William Pepper Clinical Laboratory, Phœbe A. Hearst Foundation.)

The implication of the nervous system in malaria cannot be regarded as a recent discovery. A thesis in which this subject is considered was written by Ouradou in 1851 (Mannaberg). In studying the literature we find references to paralyses believed to have been of malarial origin, and yet the nervous symptoms of malaria do not seem to have attracted attention except from a comparatively small number of observers. Gowers,[2] in his second edition, refers in a few lines to the occurrence of malarial paralysis of central origin, and he writes as though these cases had not come under his own observation. He speaks of having seen several cases of what was probably malarial neuritis. Malarial neuritis seems to have been observed by the Germans only within the present year (Baumstark, Ewald[3]).

Clinical cases of paralysis occurring in malaria are reported. A very interesting paper on this subject was published by Gibney.[4] In speaking of one of his cases he says that the toxic influence on the nerve centres at one time was so profound that neither electric current caused any reaction, and yet recovery occurred. Two of his cases presented the symptoms of acute anterior poliomyelitis.

Suckling[5] reports a case in which paraplegia occurred twice, each time a fortnight after an attack of ague, and in each attack recovery commenced on the third morning after the onset of the paraplegia, and was complete in a few hours.

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[1] The report of this case was presented in abstract at the meeting of the American Neurological Association, May, 1900, and the paper was read, by invitation, before the Section of Medicine of the Buffalo Academy of Medicine, October 9, 1900.

[2] Gowers. "A Manual of Diseases of the Nervous System," English edition, vol. i., p. 151, and vol. ii., p. 899.

[3] Baumstark, Ewald. Berliner klin. Wochenschrift, 1900, Nos. 37 and 38.

[4] V. P. Gibney. The American Journal of Neurology and Psychiatry, 1882, vol. i., p. 1.

[5] C. W. Suckling. Brain, 1888, vol. x., p. 474.

Suckling refers to a case reported by Romberg as far back as 1853. The attacks of paraplegia occurred suddenly on alternate mornings at the same hour and passed off in a few hours. Sensation was unaffected, but the sphincters were paralyzed. The attacks were soon checked by quinine. Suckling refers to similar cases reported by Harting and Erb.

A case of malarial hemiplegia, in which quinine had a remarkably beneficial effect, is reported by Pascal,[1] but no necropsy was obtained. Cases of malarial paralysis, both motor and sensory, but without necropsy, have been reported by Stockwell.[2] One of malarial paraplegia, without necropsy, is recorded by Hurd.[3] Boinet and Salebert give references to twenty-four papers in which motor disturbances of malarial origin are described, and at the Eleventh International Congress Boinet[4] said he had seen many motor disturbances in malaria[5] such as paralyses, convulsions, and choreiform movements. Csillag, also has reported cases of malarial paralysis, in some of which recovery occurred after the administration of quinine.

Laveran,[6] in his recent monograph on malaria, refers to many papers in which paludism is described as being complicated by paralysis of spinal or cerebral origin, and says that he has observed these paralyses several times. He refers to two cases which presented the symptoms of acute anterior myelitis and were apparently cases of malaria. He observed also a case of malarial hemiplegia, and in speaking of these malarial paralyses he says that they are sometimes persistent and sometimes transitory.

One of the most recent works on malaria has come from the pen of Mannaberg.[7] He also refers to a number of clinical cases of malarial paralysis, and acknowledges that most of the cases of nervous disease resulting from malaria are without any study of the lesions. Neuropathologists, he says, have treated malaria in a "stepmotherly" fashion.

J. J. Putnam observed a case (unpublished) in which temporary hemiplegia, believed by him to have been the result of malaria, occurred. The patient recovered, except that weakness and paræsthesia persisted in the thumb.

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[1] J. Pascal. Archives de Médecine et de Pharmacie Militaires, 1887, vol. x., p. 145.

[2] G. A. Stockwell. The Medical and Surgical Reporter, March 17, 1888, p. 323.

[3] A. W. Hurd. Buffalo Medical and Surgical Journal, 1888–1899, vol. xxviii., p. 19.

[4] Boinet. Eleventh International Congress, 1894, vol. iii.; Internal Medicine, p. 82.

[5] J. Csillag. Wiener med Presse, 1895, p. 1323.

[6] A. Laveran. "Traité du Paludisme," 1898.

[7] J. Mannaberg. "Die Malaria-Krankheiten," Nothnagel's "Specielle Path. und Ther.," vol. ii., Part II.

I had the opportunity to observe on one occasion recently, with Dr. C. K. Mills, a case of malaria with implication of the nervous system, in the wards of Dr. Alfred Stengel, at the Philadelphia Hospital, and I am indebted to Dr. Stengel for permission to publish the clinical notes.

The patient, a man, sixty-three years of age, previously healthy, who had been living in a malarial district and had been bitten by mosquitoes, became dizzy while walking on the street, and began to stagger, and had to grasp a pole for support. Since then he had occasionally attacks of vertigo. Since the second day of this indisposition he had a feeling of chilliness every other day about 4 P.M. His speech was slow and more hesitating than it had formerly been, and he is said to have had an intention tremor of his hands. He was weak in the lower limbs, especially below the knees, and his gait was very ataxic. The pupils were equal, and the irides reacted promptly to light and in accommodation. The splenic dulness was slightly enlarged on percussion, but the spleen was not palpable. The malarial parasites were found in the blood by Dr. Shiffert. The patient came to the hospital August 29, 1900, and was put on large doses of quinine. He was dismissed as cured on October 12, 1900. The gait had become normal, the ataxia had disappeared, the chills had ceased, but the speech was still peculiar.

We have, therefore, abundant evidence that monoplegia, paraplegia, hemiplegia, aphasia, convulsions, and various forms of tremor have been observed in persons suffering from malaria, but it is not so certain that in all the reported cases malaria has been the cause of these symptoms. The diagnosis seems to have been made most frequently from the results obtained by the administration of quinine, and in many cases the malarial organism is not even referred to; in other cases syphilis may have been, at least partly, the cause of the symptoms, and in comparatively few of these cases to which reference is made by the different writers has the malarial parasite been found in the nervous tissues. It is possible, I think, that malaria may cause paralysis; we have sufficiently carefully observed cases to warrant this belief. It is important to know in what way these paralyses are produced.

As a rule, the paralysis of malaria is not permanent; but occasionally it is, and quinine has no effect. A case of cerebral and meningeal hemorrhage, with capillary hemorrhages in the brain, occurring in a case of quotidian fever, was reported by Blanc.[1] Mannaberg[2] says that the capillary hemorrhages are more common in malaria than the large extravasations of blood, and still more common are the disturbances due to closure of cerebral or spinal vessels by infected red blood-corpuscles. Changes in the ganglion cells are supposed to occur as a result of the poison. The small cerebral vessels have been found plugged with the malarial parasites in a number of cases. The punctiform hemorrhages found in the brain, according to Bastianelli and Bignami (cited by Mannaberg), are usually in the white matter, more rarely on the border of the white matter with the cortex, and are not commonly seen within the cortex. This seems to be rather an extraordinary statement, as the cortex is better supplied with vessels. I am more inclined to accept Blanc's statement (cited by Mannaberg) that most hemorrhages in malaria occur near or within the cortex. I have found quite a number of hemorrhages in the cortex in my case.

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[1] H. Blanc. Archives de Médecine et de Pharmacie Militaires, 1887, p. 451.

[2] Loc. cit.

According to Laveran,[1] it is not uncommon to find a great injection of the meninges and of the convexity of the brain, even acute meningitis, in those who have died in delirium or coma from pernicious malarial fever. The color of the cortex and gray matter elsewhere is a deeper gray in these cases than is normal, and pigmented elements are found within the capillaries in microscopical examination. The capillaries are not always equally affected in all parts. The endothelial cells of the capillaries are often swollen, and this tumefaction aids in the formation of parasitic thrombi. Laveran makes a statement of great clinical importance. The papilla of the optic nerve, he says, has often a grayish tint, due to the presence of pigmented elements in the small vessels, and this discoloration may be detected during life. This may possibly be of value in those cases in which the parasite cannot be detected in the blood during life.

The absence of the malarial organism in the peripheral circulation is no proof of its absence elsewhere in the body. Thayer[2] says that in infections with the æstivo-autumnal variety only the earliest stages of its development are ordinarily to be found in the peripheral circulation, while occasionally, perhaps, in most severe infections prolonged examinations of the blood from the peripheral vessels reveal little or nothing.

In the discussion of a paper on the presence of the malarial parasite within the central nervous system, presented by Marinesco[3] to the Society of Biology of Paris, Laveran reiterated the statement that the parasite is found within the capillaries of the nervous system in all persons who have died from pernicious fever with cerebral symptoms.

A paper of great value by Councilman and Abbott,[4] published in 1885, gives a description of the brain and cord in two cases of malaria that would apply almost equally well to my case. This paper was one of the first in which the malarial parasite was seen within the central nervous system. As in my case, the bloodvessels under a low-power lens appeared as if they were artificially injected with a black granular mass, and there was scarcely a capillary in the gray substance of the brain that did not contain these bodies in greater or less numbers.

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[1] Loc. cit.

[2] W. S. Thayer. "Lectures on the Malarial Fevers," 1897, p. 62.

[3] G. Marinesco. Comptes-rendus de la Soc. de Biologie, 1899, p. 219.

[4] Councilman and Abbott. THE AMERICAN JOURNAL OF THE MEDICAL SCIENCES, 1885, p. 416.

More recently Ewing[1] has described cases of malaria in which the malarial parasites were present in great numbers in the central nervous system.

Thayer[2] believes that many of the cerebral symptoms of malaria may be due to a circulating toxic substance, the presence of which we cannot but acknowledge is highly probable.

The alteration of the blood occurs rapidly in severe malaria, and to this alteration, according to Laveran, are due the œdema and hemorrhages found in malarial infection. The thrombi formed by the parasites may cause foci of softening and motor paralysis if the motor areas are implicated. I have not been able to find a statement as to whether Laveran or anyone else has seen degeneration of the motor tract resulting from a lesion of malarial origin, as has been observed in the case I report.

Malarial paralysis, therefore, has been supposed by some to be the result of malarial cachexia (Gubler); by others as the result of congestion of the nervous centres (Maillot, Ouradou, Jaccoud, Grasset); by others as the result of an alteration of the blood (Rindfleisch); by others as the result of rupture of small capillary aneurisms filled with pigment (Kelsch).

Pugibet[3] quotes these opinions in reporting cases of chronic dysentery or diarrhœa with symptoms of implication of the nervous system.

The case of malaria I have to report was one with the symptom-complex of disseminated sclerosis, largely unilateral. The patient was in the service of Dr. Dercum at the Philadelphia Hospital, and to him I am indebted for the pathological material and the clinical notes. I had the opportunity to observe this patient quite frequently, and recognized the resemblance of the case to one of multiple sclerosis. He was presented by Dr. Dercum[4] before the Philadelphia Neurological Society, May 31, 1897:

H. A., white, male, aged forty years, born in Sweden, a sailor, was admitted to the Philadelphia Hospital, September 5, 1896, and died there September 23, 1899.

Family History. His mother died of phthisis; three brothers and three sisters are living and well.

Previous History. He enjoyed good health until his present trouble began. He had a chancre in 1871. In December, 1895, he suffered from headache, vertigo, drowsiness, and diplopia. At this time he lost power in the left side suddenly, without loss of consciousness. Four years previously he lost power in the right side for four weeks.

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[1] Ewing. Journal of Nervous and Mental Disease, 1899, p. 701.

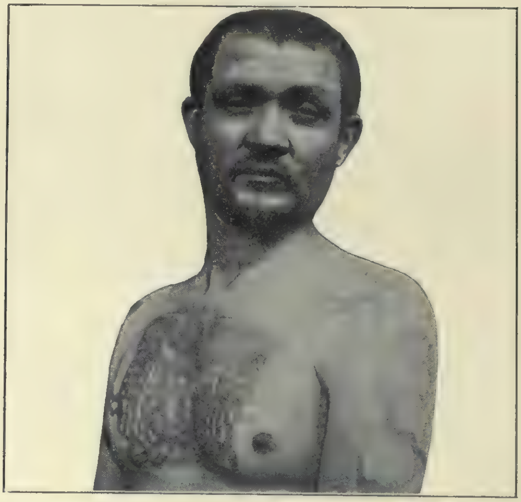
[2] Loc. cit.

[3] J. Pugibet. Revue de Médecine, 1888.

[4] F. X. Dercum. Journal of Nervous and Mental Disease, November, 1897, p. 704.

Present Condition, November 5, 1896. His sway is decidedly increased on making the Romberg test. He stands unsteadily on the right foot alone, and cannot stand on the left foot alone because of ataxia. In walking the left foot is swung awkwardly upward and outward, and strikes with the flat of the sole upon the ground. The movements of the right foot are apparently normal. When the patient lies on his back and is asked to move the legs he has marked ataxia of the left leg and a very slight degree of ataxia of the right leg. The ataxic movements of the left leg are somewhat jerky in character. The movements of precision are all well executed with the right hand. The movements of the left arm are excessively ataxic and jerky. When he is told to place a finger of his left hand upon his nose the limb is moved clumsily until it approaches the neighborhood of the nose, and then lateral or to-and-fro oscillatory movements, jerky in character, occur, becoming more intense with the degree of effort made. No tremor is observed in the right hand, but slight unsteadiness of the limb as a whole is detected. In the left hand tremor is on movement, but coarse up-and-down movements are provoked by extending the forearm with the fingers separated.

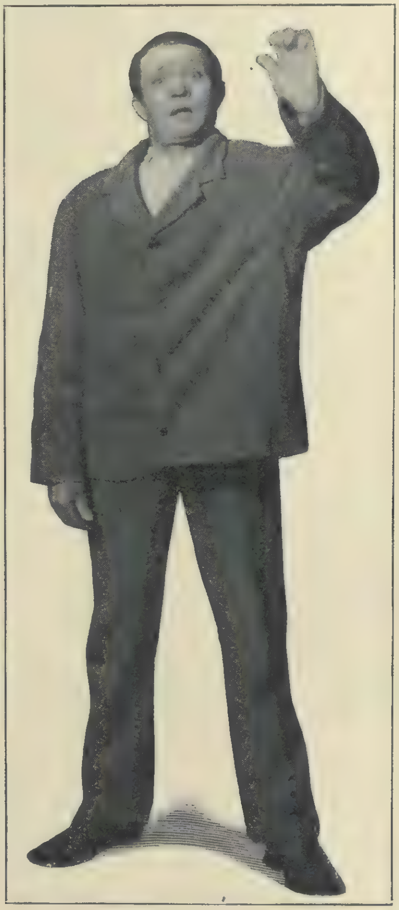
FIG. 1.



Photograph of the patient with the symptoms of disseminated sclerosis. The somnolent expression is imperfectly reproduced. (Photograph obtained from DR. C. Y. WHITE.)

Face: The man has a pronounced expression of somnolence. The eyebrows are raised, as though he were making an effort to keep awake. The lines of the face, except those of the forehead, are comparatively smooth. The face appears relaxed. The head is held slightly inclined to the right shoulder. The face is somewhat asymmetrical, the left side appearing larger. There is no sign of facial palsy and no tremor of the lips. The tongue is protruded slowly, and its movements are slightly irregular. The pupils respond normally and are equal in size.

FIG. 2.



An instantaneous photograph. The left upper limb is blurred because of the tremor, but the blurring has in large measure disappeared in the reproduction. The expression of the face is striking. (Photograph obtained from DR. F. X. DERCUM.)

The movements of the eyeballs appear to be normal. There is marked vertical nystagmus. The right eyelid seems to droop slightly, and the right palpebral fissure is much smaller than the left.

November 17, 1896. The patient has never had any bladder or rectal trouble. The sphincters are normal. He has no sensory disturbances. The reflexes:

	Right.	Left.
Knee-jerk	+	normal, possibly slightly —.
Ankle clonus	slight	none.
Elbow-jerk	+	normal, or slightly —.
Biceps-jerk	+	" " "
Wrist-jerk	+	" " "

Subjective Symptoms. H. A. has no headache at present, but says he had headache, giddiness, and ringing in the ears for five years until the fall of 1895, at which time he was relieved by medicine. He has not had convulsions or attacks of unconsciousness or pain in the bones.

Superficial reflexes: The right plantar is marked, and the left is excessively so. He has no toe reflex (by this is meant the reflex described by Sinkler, and consisting in the drawing of the lower limb upward when the great toe is forcibly flexed). The superficial reflexes of the thigh and abdomen are much increased.

Ocular examination by Dr. de Schweinitz, December 1, 1896: "The pupillary reflexes are normal. The optic examination is negative except that there is possibly slight œdema over the disk. No muscular defect is evident."

March 26, 1897. Nystagmus is present when the patient looks toward the extreme right. The right knee-jerk is very large and spastic; the left knee-jerk is normal. The ankle clonus on the right side is slight, and none is observed on the left side. The biceps-jerk and the muscle-jerks in the arms are all good. The chin-jerk is present. Sensation of the hands is normal.

October 13, 1898. H. A. was seen by Dr. Dercum, and a diagnosis of insular sclerosis was made, perhaps specific in character.

December 20*th.* H. A. fell to-day against steam-pipes and burned his right thigh on the outer side, but not seriously.

22*d.* The man is fully able to be about the ward, and has no pain.

29*th.* The ulcers are healing nicely.

September 1, 1899. The patient is up and moves about the ward daily, but is very weak and moves with difficulty. It is difficult to understand what he says, on account of scanning speech.

18*th.* He has had diarrhœa for several days, and his weakness seems to be increasing.

20*th.* He is slowly failing.

22*d.* The diarrhœa has ceased for several days, and he is very weak.

23*d.* The patient died early this morning.

The necropsy was performed by Dr. T. S. Kirkbride, Jr., and the necropsical notes were made by him:

September 23, 1899. Body of a fairly well-formed, poorly nourished male. *Rigor mortis* not present. Both layers of peritoneum smooth and glistening. Position of organs normal. The left pleural sac contains a moderately increased amount of clear, straw-colored fluid. Over the lower part of the left lobe the pleural layers are adherent. The right pleural sac contains an increased amount of fluid, but there are no adhesions. Both layers of pericardium are smooth and glistening. The sac contains a considerably increased amount of clear, straw-colored fluid.

Heart. Both ventricles contain currant-jelly clots and a small quantity of fluid blood. The valves are all normal and are not thickened. The muscle is dark brown in color and somewhat friable.

Lungs. The upper lobe of the left lung is moderately emphysematous, as is also the lower lobe at its anterior margin. On incision into the lower lobe a large quantity of brownish-yellow and reddish-brown fluid exudes. The mucous membrane of the bronchi is reddish-brown in color, and is covered by a considerable amount of mucus. Scattered foci of consolidation are found in the lower lobes. The right lung resembles the left. The œdema is less marked and foci of consolidation are not so numerous.

Spleen. The spleen is much enlarged; its capsule is tense and color dark slate; consistence soft. The cut surface shows the pulp in semifluid condition and easily scraped off in considerable quantity.

Suprarenals. Left is normal, as is also the right.

Left Kidney. The left kidney is small and its capsule is moderately adherent, leaving finely granular surface on removal. The cut surface shows the cortex broad and yellowish in color. In the pyramids are yellowish bands alternating with reddish. The consistence is perhaps slightly increased.

Right Kidney. The capsule is only slightly adherent and the surface is fairly smooth. The cortex is of moderate width and yellowish in color.

Bladder. Walls are thin, the bands of muscles standing out prominently.

Duodenum is normal.

Stomach. The mucous membrane on the summit of the folds is injected, and the surface of the membrane is covered with a mucous exudate.

Liver. The right lobe is large, the surface is smooth, and of dark slate color The cut surface is slightly uneven and granular in places in the right lobe; the parenchyma has a loose, spongy appearance (Schaumleber?).

Brain. Dura was tightly adherent over the right lobe of the cerebellum, and was, therefore, removed with the brain. The cerebrospinal fluid was increased in amount.

Pathological Diagnosis. Multiple sclerosis (?), emphysema of lungs, œdema of lungs, bronchopneumonia, acute splenic tumor, parenchymatous nephritis.

Heart weighed	370	grammes.
Left lung weighed	950	"
Right lung "	955	"
Spleen "	550	"
Left kidney "	160	"
Right kidney "	160	"
Liver "	1890	"
Brain "	1450	"

A brief abstract of the case is as follows:

H. A. was born in 1856, and had been in fairly good health, so far as can be determined, until about 1890. He had a chancre in 1871. His occupation as a sailor probably exposed him to malaria, with which he became infected. In 1891 he lost power in the right side of his body. The hemiplegia was slight and disappeared altogether in four weeks, and was not accompanied by loss of speech. It was due to organic change within the central nervous system. In December, 1895, he began to have headache, vertigo, drowsiness, and diplopia, although he had suffered from headache, dizziness, and ringing in the ears for five years, until the fall of 1895, when he was relieved by medicine. About December, 1895, he suddenly lost power in the left side of the body, but the attack of weakness was not accompanied by any loss of consciousness, and was not caused by lesion of the pyramidal tract innervating this side, as shown by the normal condition of this tract in the microscopical examination. He recovered power on this side quite rapidly, but ever since has had difficulty in walking, and has not been able to hold objects well with his left hand.

When he was examined on November 5, 1896, his sway was decidedly increased on making the Romberg test. He stood unsteadily when resting only upon the right foot, and was entirely unable to stand alone upon the left foot, on account of ataxia and not of weakness. The movements of the left lower limb were very ataxic, but those of the right lower limb seemed to be normal. He had some unsteadiness of the right upper limb on movement and very pronounced intention tremor in the left upper limb. He presented a very somnolent appearance. Marked vertical nystagmus was easily elicited. The speech was decidedly scanning. The knee-jerk was exaggerated on the right side, but was normal on the left, and ankle clonus existed only on the right side. The tendon reflexes of the right upper limb were exaggerated.

These symptoms persisted with little or no change until the patient contracted a diarrhœa, which lasted over a week and terminated in death on September 23, 1899.

The temperature-chart taken during the last few days of his life is published with this article (Fig. 3). A chart made three years previously showed a slightly subnormal temperature.

An interesting finding at the necropsy was the enlarged spleen. The diarrhœa which was so severe just before death, and which possibly caused a fatal termination by exhaustion, was probably malarial in character. The æstivo-autumnal form of parasite, according to Thayer,[1] may cause a clinical picture very closely resembling that of Asiatic cholera—*i. e.*, sudden, profuse watery diarrhœa, associated with intense prostration, the patient sinking into an algid condition. This attack may be rapidly fatal, and usually is so without treatment.

The right crossed pyramidal tract in the case H. A. is moderately sclerotic throughout the spinal cord; this sclerosis is by no means intense, but it is unmistakable. It is sufficiently pronounced to indicate that the focal lesion in the pyramidal tract producing the secondary degeneration could not have been very extensive. The sclerosis consists merely of slightly thickened bands of neurogliar tissue here and there within the right crossed pyramidal tract, and seems to be especially marked about the small vessels of this tract, although it is also found apart from the vessels. The cells of the anterior horns appear to be normal by the ammonium-carmine stain; they are of normal shape and have centrally situated nuclei. The left direct pyramidal tract presents no distinct evidences of sclerosis. The right anterior horn is smaller than the left throughout the spinal cord, but it does not seem probable that the relative smallness of the right anterior horn could result from the very moderate degree of degeneration of the right crossed pyramidal tract. The cells in the right anterior horn are about as numerous as those in the left. No recent degeneration of the spinal cord is found by the Marchi method. An area of slight sclerosis is observed in the outer portion of the middle third of the foot of the left cerebral peduncle. A small hemorrhage is found in the posterior limb of the left internal capsule. This hemorrhage has the appearance of one of recent origin. The sclerosis of the pyramidal tract from the left hemisphere cannot be traced above the lower part of the posterior limb of the left internal capsule. Numerous small recent hemorrhages are found in the left paracentral lobule and other parts of the cortex, and occasionally the malarial parasites are found within these hemorrhages. The giant cells of the paracentral lobule appear to be normal with the ammonium-carmine stain. The small bloodvessels throughout the brain and cord are filled with the malarial parasites.

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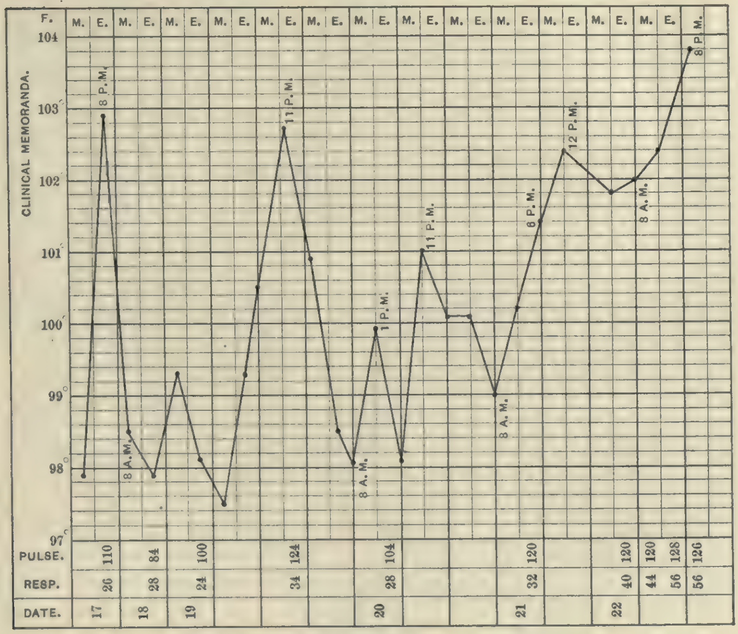
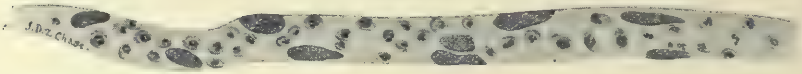
[1] W. S. Thayer. "Lectures," p. 152.

FIG. 3.



Transitory paresis of the right half of the body, and four years later a similar hemiparesis of the left side, in connection with the other symptoms, made the existence of disseminated sclerosis seem very probable. Transitory paralysis is well known as a sign of this disease. The paralysis could hardly have been the result of syphilitic disease of the nervous system, because no lesions resembling those of syphilis were detected with the microscope. Whether the right-sided paralysis was greater in intensity than that observed on the left side I cannot say, but I find sufficient changes within the central nervous system to explain the right hemiparesis. The motor tract from the left hemisphere is partially sclerotic, and this sclerosis can be traced throughout the right crossed pyramidal tract into the left cerebral peduncle and lower part of the left internal capsule, and is lost within the left internal capsule. The sclerosis was too slight to cause a persistent and intense paralysis of the right side of the body, but it was sufficient to produce distinct symptoms. The man stood unsteadily when resting upon the right foot, and this was not due to ataxia, which did prevent him from standing upon his left foot alone. Notwithstanding the moderate degree of sclerosis of the motor tract from the left cerebral hemisphere, the movements of the right foot and leg appeared to be normal. Exaggeration of knee-jerks and ankle clonus on the right side were further evidence of the implication of the right crossed pyramidal tract. On the left side the knee-jerk was normal and ankle clonus was absent, and there was no sclerosis in the left crossed pyramidal tract.

FIG. 4.



Malarial parasites within a capillary of the central nervous system, as shown in one focus. The full number of parasites in any vessel can be determined only by changing the focus.

The cause of the partial sclerosis of the motor tract from the left hemisphere was probably the occurrence of small hemorrhages. I have found hemorrhages of recent formation within the left internal capsule in its posterior limb and in many parts of the cerebral cortex, and it seems probable that if recent hemorrhage occurred similar lesions may have developed at earlier periods. In the seven or eight years which elapsed between the attack of right hemiplegia and death all evidences of these hemorrhages, except the slight secondary degeneration and sclerosis, had disappeared. The left cortex showed no lesions except the closure of the capillaries by the parasites and recent hemorrhages, and this explains the absence of aphasia in the right hemiparesis.

I have found no explanation for the transitory weakness of the left side of the body. This also may have been due to small hemorrhages, but if so the hemorrhages were either not directly in the motor tract or were not sufficient to cause secondary degeneration.

This patient presented the clinical picture of disseminated sclerosis. His symptoms of the disease were:

1. A very marked intention tremor of the left upper limb. As the left hand approached the desired object the tremor became excessive and exactly like that seen in disseminated sclerosis.
2. Marked ataxia of the left lower limb. The left foot was swung awkwardly upward and outward in walking, and struck with the flat of the sole upon the ground. When the patient lay upon his back he showed marked ataxia in movements of the left lower limb. The ataxia of the left lower limb was so great that the patient was unable to stand upon this limb alone.
3. Transitory hemiparesis, first of one side of the body, then of the other.
4. Headache, vertigo, drowsiness, and diplopia.
5. Marked vertical nystagmus readily elicited.
6. Speech that was distinctly scanning.
7. Tendon reflexes exaggerated on the right side, with ankle clonus on the same side.

A few cases of disseminated sclerosis attributed to malaria are reported, but none with necropsy as far as I have been able to study the literature.

Canellis[1] reports the case of a man, aged forty-two years, who had had intermittent fever and malarial cachexia. He believed that malaria was the cause of the symptoms in the typical clinical picture of disseminated sclerosis observed in this case. Quinine had no effect. No finding of the parasite in the blood is reported and no necropsy was obtained, as the man was still living at the time the paper was written. Boinet and Salebert[2] refer to pseudodisseminated sclerosis from infection, described by Kahler and Pick, and by Marie, and they report a case of malaria which resembled one of disseminated sclerosis. There was no necropsy. This patient, a man, had paraplegia with preservation of the reflexes, tremor of the head and of the lower limbs on voluntary movement.

In a case of malaria reported by Triantaphyllidès[3] the speech was slow and scanning and "absolutely characteristic," according to the author, of disseminated sclerosis. In repose the patient, a man, aged twenty-six years, who had had malarial fever until five days previously, presented no tremor, but in attempting to carry the hand to the mouth tremor appeared in the hand, and increased in amplitude if the movements were continued. Distinct nystagmus was present. The tendon reflexes of all the extremities were exaggerated, and vertigo was complained of. The liver and spleen were enlarged and malarial parasites were found in the blood. This was the patient's condition on October 13, 1892. Quinine was administered. On October 26th the signs of disseminated sclerosis were much less distinct, and by November 11th they had disappeared. This was regarded as indisputably a case of malaria. Triantaphyllidès remarks that it would be interesting to know whether cases similar to his, not treated, would terminate in true disseminated sclerosis. To this question the study of the case I report permits the reply that the symptoms of disseminated sclerosis from malaria may probably exist for at least eight or nine years, and possibly longer, without any formation of disseminated sclerotic foci in the central nervous system.

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[1] S. Canellis. Gazette Hebdomadaire de Médecine et de Chirurgie, second series, 1887, vol. xxiv., p. 554.

[2] Boinet and Salebert. Revue de Médecine, 1889, p. 933.

[3] Triantaphyllidès. Archives de Neurologie, 1893, vol. xxvi., p. 232.

Torti and Angelini[1] observed two cases of chronic malaria in which the symptoms of disseminated sclerosis were seen during the apyrexia. One case was as follows: A man, aged twenty-one years, after having had malarial fever of irregular type for three months, in October and November had vertigo and vomiting; later he had weakness of the legs, scanning speech, exaggerated tendon reflexes, intention tremor, and ataxia of the upper limbs, slow reaction of the iris, and slight nystagmus. Temperature and sensation were then normal. The vertigo and vomiting persisted and increased in intensity. The malarial parasites were found in the blood. After administration of quinine and Fowler's solution the symptoms became much less marked, and the parasites disappeared from the blood. At the end of December the patient again developed fever, and after a few days had spastic paresis and ataxia of the extremities, nystagmus, tremor, exaggerated reflexes, scanning speech, headache, and vertigo; and the malarial parasites were again found in the blood. The symptoms again disappeared in great measure.

The other patient, a man, aged twenty-two years, with normal temperature, but who was very anæmic, had headache, vertigo, scanning speech, nystagmus, intention tremor of the hands, exaggeration of the tendon reflexes, but normal sensation. These symptoms developed in November, after he had had malarial fever in August and September. Malarial parasites were found in the blood. After treatment for three weeks with quinine and Fowler's solution the patient was discharged cured.

Two cases with the symptoms of disseminated sclerosis, in which the malarial parasite was found in the blood, were reported by Bignami and Bastianelli.[2]

Torti and Angelini believe that the cause of the symptoms in disseminated sclerosis occurring in malaria is an intoxication of the nerve centres, and not vascular disease.

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[1] Torti and Angelini. Abstract in Neurologisches Centralblatt, 1893, p. 858.

[2] Bignami and Bastianelli. Cited by Torti and Angelini.

In 1895, Triantaphyllidès[1] published three cases of malaria with the symptoms of disseminated sclerosis. Whether or not his former case was included in these I cannot say. He found the parasites in the blood.

J. J. Putnam[2] says he saw a case that suggested a relation between malaria and disseminated sclerosis. A man, in middle life and of good health, was attacked suddenly with characteristic and progressive intention tremor and scanning speech immediately after a sharp malarial attack. Under treatment by arsenic there was a slight improvement, but for the most part the symptoms persisted.

It is well known that Marie[3] has regarded infectious diseases as a cause of disseminated sclerosis, and the symptoms of disseminated sclerosis occurring in malaria might offer some support to his views, seeing that no necropsies have been obtained, with the exception of the one I now report. The symptoms of disseminated sclerosis occurring in malaria usually disappear after the administration of quinine, and could not, therefore, be due to disseminated foci of sclerosis. Malaria is given by a number of writers as a cause of disseminated sclerosis, apparently without any knowledge on the part of some that this malarial disseminated sclerosis is probably a pseudosclerosis. Oppenheim,[4] however, has clearly recognized this fact, for he mentions that a form of pseudosclerosis curable by quinine is said to result from malaria.

It is interesting to know that symptoms resembling those of tabes are said to have been due to malaria (Mannaberg), and Dr. C. K. Mills has mentioned to me a case which seemed to be of this character.

The patient H. A. had excessive ataxia and tremor in the left extremities, although he had a very slight degree of ataxia in his right lower limb and some unsteadiness of the right upper limb. The difference between the ataxia of the limbs of the two sides of the body was most striking. The explanation of this must be found in the moderate sclerosis of the motor tract from the left cerebral hemisphere. In the discussion following the presentation of the patient by Dr. Dercum at a meeting of the Philadelphia Neurological Society, Dr. Wharton Sinkler[5] said he had had a patient under his care who had disseminated sclerosis, with marked intention tremor on both sides. This man became paralyzed on the left side. He partially recovered from this paralysis, and the tremor disappeared entirely on the hemiplegic side, while it remained unchanged on the other.

Mannaberg[6] saw a patient with paralysis of the right extremities from a lesion in the pons. This man contracted malaria, and during the chill is said to have had tremor only on the left side.

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[1] Triantaphyllidès. Abstract in Revue de Médecine, 1896, p. 877.

[2] J. J. Putnam. THE AMERICAN JOURNAL OF THE MEDICAL SCIENCES, March, 1895.

[3] P. Marie. Progrès Méd., 1884, vol. xii., p. 287.

[4] H. Oppenheim. "Lehrbuch der Nervenkrankheiten," second edition, p. 262.

[5] Sinkler. Journal of Nervous and Mental Disease, 1897, p. 706.

[6] Loc. cit.

In the case H. A. the malarial parasites were as numerous on one side of the central nervous system as on the other. There must have been an abnormal irritation of centres and tracts, and the tremor might have been expected to be equally great on the two sides of the body. One pyramidal tract was partially sclerotic, and the limbs innervated by this tract showed scarcely any ataxia or tremor. The sclerosis must, therefore, have counteracted the irritation produced by the parasites. When movements were made with the left limbs the normal flow of impulses was disturbed. The centres were probably in an abnormal condition of irritation, and the proper degree of muscular contraction could not be gauged, hence the intention tremor and ataxia. The centres for the right half of the body were doubtless in a similar state of abnormal irritation, and excessive and inco-ordinate impulses were sent out from these centres, but excessive action was checked by the degeneration of some of the motor fibres.

We should not speak of tremor in disseminated sclerosis, according to Strümpell,[1] but should describe the disturbance of voluntary movements as ataxia. On the other hand, Oppenheim[2] says that the tremor of multiple sclerosis is so peculiar as to be almost pathognomonic of the disease.

Leyden and Goldscheider[3] can find no satisfactory explanation for intention tremor. According to Charcot, it is due to loss of the medullary sheaths of the nerve fibres and the disturbed conduction of impulses thereby. Erb has been more inclined to attribute the cause to certain locations of the lesions. Leyden and Goldscheider think that foci of sclerosis in the cerebrum and pons are especially liable to cause this form of tremor, although it may possibly be due to lesions of the spinal cord and medulla oblongata. The truth is, we do not understand the cause of intention tremor, and no theory is fully satisfactory.

It might be thought extraordinary that the malarial organisms should have remained so many years in the person of H. A. and have caused no more characteristic manifestations of malaria; and I do not assert that they were present during all this period, but no other cause for the symptoms of disseminated sclerosis was found by the microscopical examination, and it is possible that the parasites were not always as numerous as they were at the time of death. Malaria sometimes persists in spite of treatment, though the symptoms may cease for a time, and a return of the symptoms is not necessarily a proof of reinfection. The case I report has much in common with some of the other cases of malaria with the clinical picture of disseminated sclerosis, and such symptoms as were present in H. A. must have had a very definite cause. Some statements made by Thayer[1] throw light upon the question :

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[1] Strümpell. "Lehrbuch der speciellen Pathologie und Therapie," vol. iii.

[2] Oppenheim. "Lehrbuch."

[3] Leyden and Goldscheider. Nothnagel's "Specielle Pathologie und Therapie," vol. x., p. 463.

"Golgi long ago pointed out, as a regular rule, that the severity of the symptoms in malarial fever was to a certain extent in direct relation to the number of parasites present, and clinical experience has tended largely to support this view. . . . The æstivo-autumnal organism often undergoes the greater part of its development within certain special organs, and this localization of the parasite may differ materially in different cases. Thus, while in many cases the parasite may be found with equal frequency in all internal organs, in others certain special parts may be involved. In some instances the spleen, in other *parts of the central nervous system* [italics are mine], in others the gastro-intestinal tract, may be the main seat of the infection. In these cases, as one might naturally expect, the clinical symptoms often point directly to the seat of localization." (Page 146.)

"In a certain number of instances malarial infections may cause distinct symptoms, with little or no fever. . . . Usually the fever is practically absent, the temperature really being subnormal during the greater part of the time." A chart in the case H. A., taken three years before death, shows a subnormal temperature. I quote further from Thayer: "We have observed the same condition in a number of instances of æstivo-autumnal infection. These cases may show for some time a normal or even subnormal temperature, with more or less subjective symptoms. These symptoms are especially likely to be nervous —severe headache, neuralgias, and sometimes, indeed, other interesting nervous phenomena. In several instances the patients showed, beside headache, a sensation of dizziness, together with a markedly unsteady ataxic gait. The blood showed typical æstivo-autumnal organisms, both small amœboid, intracorpuscular bodies, and crescentic and ovoid forms." (Page 174.)

The quotations are sufficient to show that it is possible that in the case H. A. the malarial parasites may have been present during many years only in parts of the central nervous system, and in smaller number than at the time of the patient's death ; that the absence of fever and of periodic attacks, and the subnormal temperature observed three years before death do not militate against the diagnosis of malaria ; and that the symptoms presented by H A. are such as are known to occur in the larvated forms of malaria. The long duration of the symptoms is remarkable ; but who will venture to fix a definite limit of time to symptoms of the larvated forms of malaria, especially when quinine is not administered ?

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[1] W. S. Thayer. "Lectures on the Malarial Fevers."

It might be suggested that the case was one of hysteria, with malarial infection occurring a short time before death. No one, I think, who saw the case regarded it as one of hysteria. The somnolent expression of the man was so extraordinary that should I again observe a patient with a similar expression I should at once think of the possibility of malarial infection. The expression might well be the result of invasion of the brain by the parasites. The slight but unmistakable sclerosis of the right crossed pyramidal tract, and the well-defined small area of sclerosis of the outer part of the middle third of the left cerebral crusta, can best be explained as the result of one or more small hemorrhages of ancient date in the left motor tract, similar to those of recent date found in many parts of the central nervous system. The presence of altered blood pigment confirms this view. It would be difficult to explain this slight sclerosis of one motor tract in any other way, and the only apparent cause for these hemorrhages is in the presence of the parasites. No lesions resembling those of syphilis can be found anywhere.

Torti and Angelini[1] distinguish clinically three forms of malaria with symptoms of disseminated sclerosis:

1. Cases in which the symptoms of multiple sclerosis are transitory and are present only during the attack of malarial fever.

2. Cases in which the symptoms of multiple sclerosis appear after the fever and are of varied duration.

3. Cases in which the symptoms of multiple sclerosis appear suddenly, without any fever. The last must, therefore, be a larvated form of malaria.

The few studies on the condition of the nerve cells in malaria which have been made indicate that little alteration of these cells occurs. It is true that Monti found certain alterations with the silver stain, but this method is not one of the best for the study of pathological changes. Laveran[2] says that the nerve cells are usually unaltered, and Marinesco[3] was unable to find important lesions of the nerve cells. A few were altered, and this alteration he thought might be due to the very advanced age of the patient. Marinesco was also unable to find the parasites outside of the bloodvessels except in some small hemorrhages, and a similar statement may be made in regard to the sections studied by me. I have not been able to find any distinct alteration of the nerve cells by the ammonium-carmine stain, and it seems probable that if any changes of importance had existed during a malarial infection of many years they would have been detected by this method. The material was hardened in Müller's fluid, and I was, therefore, prevented from using the Nissl stain.

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[1] Loc. cit.

[2] Loc. cit.

[3] Loc. cit.

The great majority of the cases of malaria with nervous symptoms are, according to Mannaberg,[1] due to the æstivo-autumnal variety of the parasite, and Thayer[2] says that the more severe æstivo-autumnal fevers of Rome are much more acyclical in their manifestations, tend frequently to become pernicious, and are more resistant to quinine. This form of malarial fever is chiefly characteristic of intensely malarious districts, particularly of those regions in the tropics where the pernicious fevers are common. The æstivo-autumnal form was also found by Ewing in some of his cases of implication of the nervous system in malaria, and it is this form which is present in the case H. A. In my preparations the pigment is found at the centre of the parasite, which, according to Thayer,[3] is indicative of full development of the organism. It is no exaggeration to say that every capillary of the central nervous system is filled with the organisms, so that the appearance under a low power is like that presented by injection with some black powder. The small vessels of the pia also contain the parasites.

There could be no doubt that these organisms found within the central nervous system were the malarial parasites, but the determination of the variety was more difficult, and I am, therefore, much pleased to have the opinion of Dr. Alfred Stengel and Dr. W. S. Thayer, both of whom examined my sections, that these parasites were of the æstivo-autumnal form.

The case shows that the symptoms of disseminated sclerosis may result from irritative vascular lesions, or imperfect nutrition, or poisoning of the nerve cells, without the formation of multiple sclerotic foci. Multiple sclerosis is chiefly a disease of inco-ordination. Ataxia, intention tremor, scanning speech, and nystagmus are all symptoms of inco-ordination, and it would seem that this inco-ordination may be caused either by the production of abnormal impulses from irritation, as in my case, or by the partial arrest of normally produced impulses in the multiple sclerotic areas of true insular sclerosis.

I found groups of bacilli within the vermis of the cerebellum, and only within this part. Possibly these were of post-mortem origin, but it is singular that they were seen only in the vermis. The malarial bacilli described by Klebs and Tommassi Crudeli in 1879 are not accepted at the present day as the cause of malaria.

[1] Loc. cit. [2] Loc. cit. [3] Loc. cit., p. 67.

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CEREBELLAR LESIONS WITHOUT CEREBELLAR SYMPTOMS.[1]

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[From the Wm. Pepper Clinical Laboratory (Phœbe A. Hearst
Foundation).]

Remarks by Dr. W. G. Spiller.

The most extraordinary sclerosis of the cerebellum that I have ever observed was in a brain removed by Dr. H. W. Cattell, and reported by me with a microscopical study in the English journal *Brain*, Part LXXVI, 1896. The entire cerebellum in that case measured in its greatest lateral diameter 1 11-16 inches. I never saw the patient during his life, from whom this specimen was removed, but in the notes obtained from the case-books of the Pennsylvania Training School for Feeble-minded Children the boy is said to have had inco-ordination of gait, peculiar speech, vertigo and internal strabismus. The cerebellum, though extremely diminutive, had all the parts usually present in this organ, but a sclerotic area was found in each cerebellar hemisphere. There are very few cases of such intense hypoplasia of the cerebellum reported in the literature.

One lobe of the cerebellum is occasionally atrophied as a result of some lesion in the opposite cerebral hemisphere, because each cerebellar lobe is connected with the opposite cerebral hemisphere by both the anterior and middle cerebellar peduncles. A little more than a year ago I removed a brain in which this secondary atrophy of the cerebellum was very marked. The case was one of right internal hydrocephalus, and the right cerebral hemisphere was a mere sac. The left cerebral hemisphere was normal, but the left cerebellar lobe was much smaller than the right cerebellar lobe, and yet not abnormally hard.

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[1] Read before the Path. Soc. of Philadelphia, March 28, 1901.

In the specimen given to me by Dr. Wadsworth (Case 3 of this paper), the two cerebral hemispheres are of equal size, but the left cerebellar lobe is much smaller than the right, and is distinctly harder to the touch. The left cerebellar lobe measures 4.5 cm. transversely, and the right measures 6 cm. The various parts of a normal cerebellar hemisphere are present, but not nearly so well developed as in the right cerebellar lobe, and the hypoplasia is equally intense in all parts of the left lobe. The zona granulosa and zona molecularis are abnormally narrow, and it is difficult to find the Purkinje cells; indeed, in the greater part of the sections I have examined these cells are absent. The left corpus dentatum is very small, and the nerve cell-bodies within it are atrophied. The entire left cerebellar lobe has a very dense structure under the microscope, but I have not found any portion of it in which the nervous tissue is destroyed. The right inferior olive is much smaller than the left (Fig. 4), because the right inferior olive is in connection with the left cerebellar lobe, by means of the cerebello-olivary fibres, which are said to arise in the Purkinje cells, and these cells in the sections examined by me were absent. The left inferior cerebellar peduncle is probably smaller than the right, although my sections are from a little higher level on the right side than on the left. The middle and anterior cerebellar peduncles are not strikingly abnormal, to which fact is probably due the normal size of the right cerebral hemisphere.

The sclerosis that occurs in the central nervous system is sometimes very perceptible to the touch, but the results of a microscopic study are not always such as we might expect from a gross examination of the tissue. This has been emphasized recently in the report of a case of diffuse sclerosis by Hugo Weiss.[1] Although the consistency of brain and spinal cord in his case was increased by palpation, very little that was abnormal was found in microscopical sections, except in the spinal cord, where the amount of neuroglia was excessive. The diffuse sclerosis is believed to be the end product of a chronic inflammatory process, with implication of the vessels and proliferation of the glia. The vascular changes may be the first stage in the process. A large portion of brain or cord may be implicated in this diffuse sclerosis, and the lesions in these cases are not essentially different from those where only a small portion of the central nervous system is sclerotic. The process may either be of intrauterine origin or be acquired later in life, and it is not improbable that syphilis is a cause, and in the specimen removed by Dr. Wadsworth there were some lesions in the liver that may have been syphilitic. The proliferation of the glia has received a careful study from Sailer.[2] He concluded that there is a morbid process, of unknown origin, probably commencing before birth and after the seventh month of fetal existence, characterized by a hyperplasia of the neuroglia cells and fibres, and leading to gradual atrophy of the nerve-fibres and the nerve cell-bodies, and associated with vascular changes of doubtful nature.

The cerebellum, so far as we understand it, does not possess distinct centres, as does the cerebrum, and its chief function seems to be that of a regulator of co-ordinated movements. It assists the cerebrum, and, from its close anatomical connections with the latter, must be an organ of considerable importance.

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[1] Hugo Weiss. Obersteiner's Arbeiten, Vol. 7.

[2] Sailer. Journal of Nervous and Mental Disease, No. 6, 1898, p. 402.

The view is held by some that motor tracts may have a circuitous route through the cerebellum, but few facts can be offered in justification of such an opinion as this. The function of the cerebellum can be best determined by a study of the cases of sclerosis of the organ, as this form of pathological change produces symptoms more sharply defined than any other. Tumors or abscesses may cause symptoms by pressure on parts not actually injured, and the symptoms so produced may be attributed to the cerebellum; these cases therefore are useless for a study of cerebellar function. Suitable cases of cerebellar lesions with necropsy are not numerous, but André Thomas,[1] in his thesis on the cerebellum, published in 1897, collected from the literature some seventeen cases, and from the symptom-complex observed in these described the symptoms attributable to defect of a part of the cerebellum. The cases are those reported by Meynert, Fiedler, Clapton, Pierret, Kirchoff, Huppert, Fraser, Claus, Borell, Schultze, Hammarberg, Bind, Nonne, Menzel, Royet and Collet, Arndt, and Spiller. All these were cases of atrophy or sclerosis implicating the entire cerebellum, and a study of these cases shows that on the integrity of the cerebellum usually depends the co-ordination of movements when the individual is standing, but to a much less extent when he is lying down. Lesion of the cerebellum does not cause distinct paralysis, and the reflexes may be exaggerated or normal. Romberg's sign is not present, *i. e.*, inco-ordination is not increased by closure of the eyes. Speech is scanning or explosive. Ocular disturbances, vertigo or vomiting may occur.

Lesions confined to one-half of the cerebellum are less likely to cause symptoms than when they implicate the entire cerebellum, and yet symptoms from unilateral lesions have been observed, according to

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[1] Thomas, Le Cervelet, 1897.

Thomas, by Andral, Thierry, Meschede, Lallement, Leveque, Kirchoff, Hitzig, and Amaldi. It is questionable whether Hitzig's case should be placed in this list. If the injury to the cerebellum occurs early in life and is of slow development, or if the condition is one of arrested development, symptoms may be absent, probably because the functions of the cerebellum have been assumed by other portions of the brain. The removal of one lobe of the cerebellum in animals does not usually cause persisting disturbances of function. A number of cases of great defect of the cerebellum with few or no symptoms, have been reported. The most extraordinary case of cerebellar defect on record is one reported in 1831 by Combette.[1] The development of the child was slow, and the age of five years was attained before she was able to support her weight on her lower limbs. She was of feeble intellect and weak in the extremities, so that she often fell. A gelatinous membrane was found in the place of the cerebellum, and there was no trace of the pons. We can hardly be certain of the extent to which the absence of the cerebellum was responsible for these symptoms. I have seen very similar symptoms in cases in which the cerebellum seemed to be of normal development.

I am unable, from Duguet's report[2] of the first case in his paper, to say whether disturbance of co-ordination was present or not. The cerebellum was only about half the normal size, and weighed 85 grams.

In the case observed by Otto[3] the movements were vigorous and co-ordinated, but mental defects were very evident. The cerebellum was only 5 cm. in width, and proportionally small in its other dimensions.

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[1] Combette. Revue Médicale, Vol. 2, 1831, p. 57.

[2] Duguet, Bulletins de la Soc. Anat. de Paris, 1862.

[3] Otto. Archiv für Psychiatrie, Vols. 4 and 6.

In F. Fischer's case[1] the cerebellum weighed 78 grams, and the normal average weight of this organ as given by him is 150 grams. No symptoms indicating the existence of this anomaly were detected during the life of the patient.

Hitzig's patient was a woman who, according to the statement of the patient's mother, had never had disturbance of motion, and had learned to walk at an early age and could dance. When she came under Hitzig's observation she had paretic dementia, and the disturbance of co-ordination she then showed was probably a sign of this disease. The right cerebellar lobe was a mere rudiment, and the vermis was very imperfectly developed. A depression was found in the position of the left lower olive.[2] Hitzig thought that the condition of the cerebellum was one of arrested development.

I have been unable to obtain the journal containing the report of Ingels' case, but according to the abstract given by A. Thomas, the man was an imbecile, without inco-ordination of movement. The cerebellar lobes and inferior vermis were very small.

I must depend also on Thomas' abstract of Shuttleworth's case, but I have been able to obtain the original reports of the other cases mentioned in this paper. Shuttleworth's patient was a girl with phthisis, fifteen years of age at the time of death. No peculiarities of movement were observed during her life, but she had great general weakness and tremor of the hands and arms. The cerebellum was exceedingly diminutive.

In a case reported by Doursout[3] (Case 4), disturbance of locomotion did not exist. The cerebellum

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[1] Fischer. Archiv für Psychiatrie, Vol. 5.

[2] Hitzig Archiv für Psychiatrie, Vol. 15, p. 266, VIII. Wanderversammlung der Südwestdeutschen Neurologen und Irrenärzte in Baden am 16 und 17 Juni 1883.

[3] Doursout Annales Médico-Psychologiques Septième Série 13, 1891.

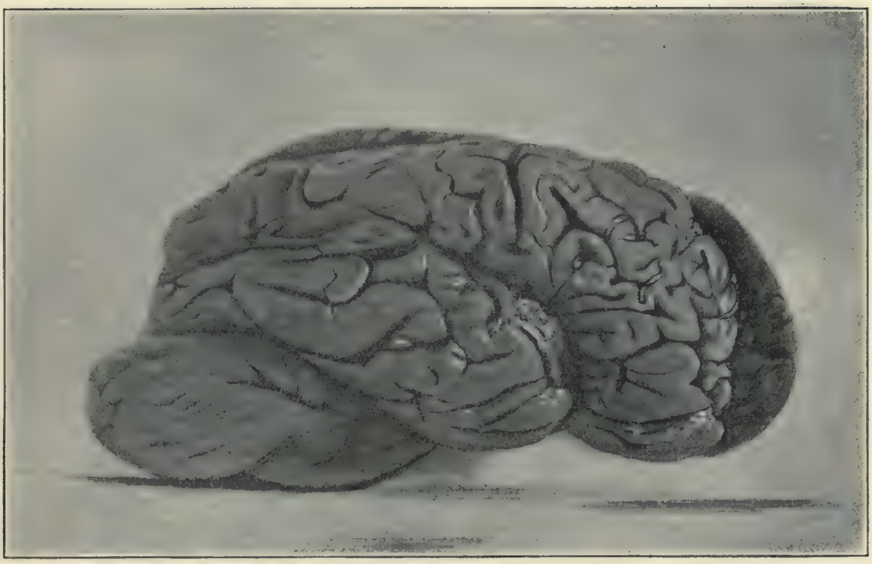

FIG. 1.—Brain from a case of internal hydrocephalus of the right cerebral hemisphere. The right cerebral hemisphere was much smaller than the left, and was merely a thin-walled sac.

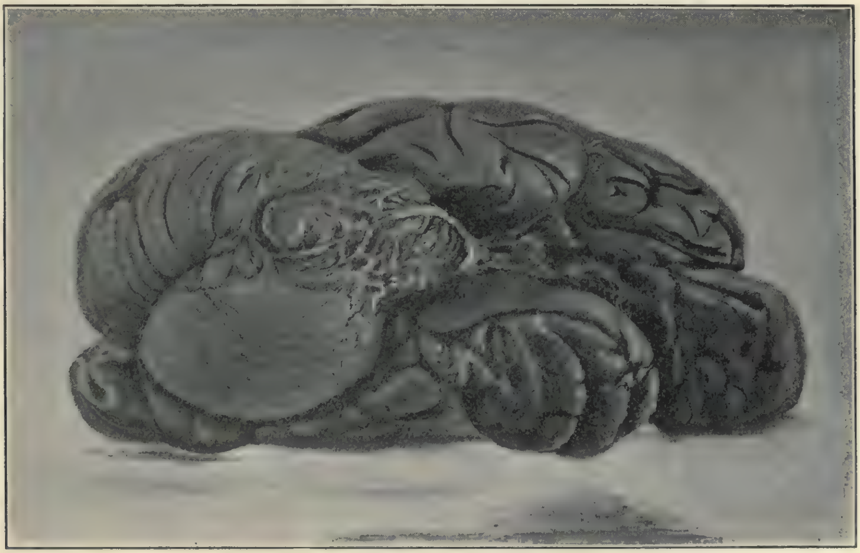

FIG. 2.—Basal aspect of brain from a case of internal hydrocephalus of the right cerebral hemisphere. The left lateral lobe of the cerebellum is much smaller than the right.

weighed 80 grams, which, according to Doursout, was a little more than half the normal weight.

Ferrier[1] reports the following interesting case: A girl, fifteen years old at the time of death, had been somewhat weak in intellect, and her articulation had been somewhat indistinct. No deficiency had existed as regards her sensory faculties, general or special, and the only peculiarity observable in her motor power had been a general muscular weakness and tremor of the hands when she was using them, but this was attributed to the debility associated with her phthisical condition. She had been able to walk well and steadily, though she had never been known to run. The cerebrum was normal, but the cerebellum was of the most diminutive character. The left lobe was a mere papilla, the vermiform process a minute nodule, obscurely marked with laminæ, while the right lobe, which constituted the main portion, was only half a square inch in superficial area, and only a quarter of an inch in thickness at its base. This Lilliputian lobule had, however, the normal laminated appearance and structure. The pons was indicated by only a few transverse fibres, which barely concealed the pyramidal tracts in their course from the foot of the cerebral peduncle. The corpora quadrigemina had a normal size and appearance. The olivary bodies of the medulla oblongata were only obscurely indicated. With the exception of the cerebellum and its peduncles, which were reduced to insignificant dimensions, the rest of the brain and all the cranial nerves were perfectly normal in appearance.

These were congenital or early acquired defects of the cerebellum, and therefore less likely to cause symptoms than tumors or hemorrhages developing after the cerebellum is formed, and at a time when

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[1] The functions of the brain, second edition. David Ferrier, p 180.

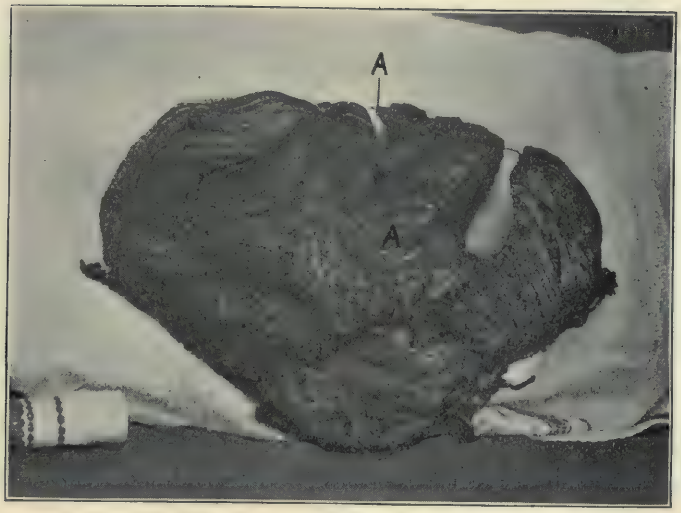

FIG. 3.—Sclerosis of the left cerebellar lobe (Case 3).

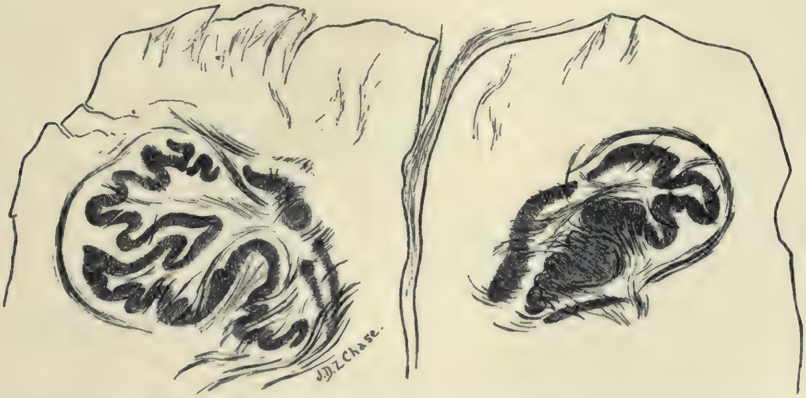

FIG. 4.—Atrophy of the right inferior olive from sclerosis of the left cerebellar lobe (Case 3).

the vicarious action of another part of the brain is less likely to occur; and yet in a case reported by Becker,[1] vertigo, paralysis, disturbance of sensation, headache and ataxia are said to have been absent, and during the year preceding the death of the patient, and at a time when she was under the observation of Becker, she appeared as a normal person. Two cysts were found in the cerebellum, and the only parts of the vermis persisting were the lingula, lobus centralis, uvula, and nodulus, while the monticulus, folium cacuminis, tuber valvulæ and pyramis were destroyed. A large part of the vermis therefore had disappeared, and yet no symptoms of cerebellar lesion had been detected. The cysts were regarded by Becker as of hemorrhagic origin and as having existed at least months, and possibly years, before the death of the patient. He refers to three cases reported by Jager as instances of disease of the vermis without ataxia, and reports two cases that are also mentioned by Schomerus. In one there was no ataxia, although a tumor and cyst had destroyed a large part of the cerebellum and implicated the vermis. In the other case weakness of the left upper and lower limbs and some awkwardness of movement existed, and yet Becker distinctly states that no inco-ordination was present. A tumor compressing the vermis was found. Compression of nervous tissue by a tumor I have found in some cases to cause relatively few symptoms, fewer than when the nervous tissue is actually destroyed, and it is not so surprising that in the case of tumor on the corpora quadrigemina (Case 2) cerebellar symptoms were not detected, although the left lobe of the cerebellum was much compressed.

Inco-ordination is usually present in tumor of the vermis, and it has been supposed that the posterior

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[1] Becker. Virchows Archiv, Vol. CXIV, 1888.

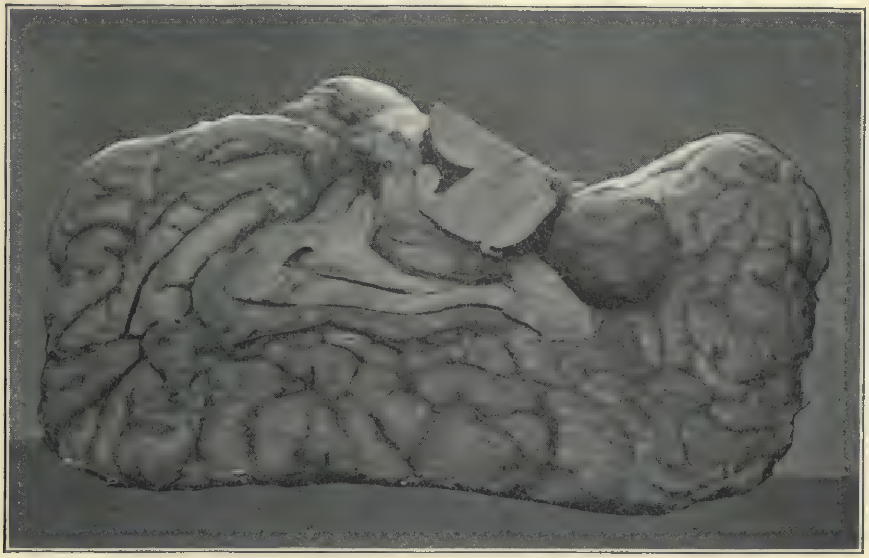

Fig. 5.—Tumor on the corpora quadrigemina, compressing the left lateral lobe of the cerebellum. The cerebral hemispheres have been separated, and the cerebellum and caudal portion of the pons have been cut away (Case 2).

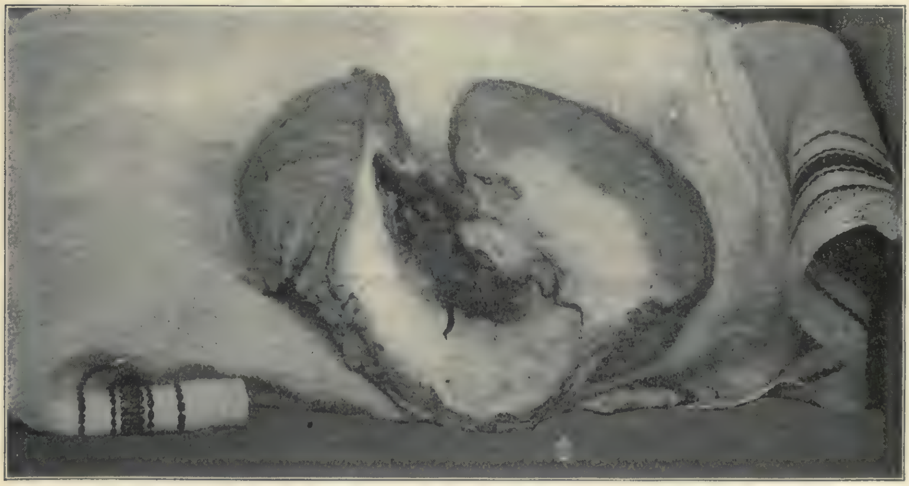

Fig. 6.—Almost complete destruction of the vermis by a cystic glioma (Case 1).

part of the vermis is more important for the preservation of co-ordination than the anterior, and yet in the specimen given to me by Dr. Robertson (Case 1) the vermis was almost destroyed by a glioma and cyst in its posterior as well as its anterior portion. Glioma is not a very rare tumor of the cerebellum.

Leimbach[1] observed a case in which a tubercle was found in the vermis and had probably existed a long time without causing any symptoms indicative of a cerebellar lesion. He offers, as an explanation for this absence of cerebellar symptoms, the fact that in all the cases in which ataxia existed the injury of the cerebellum was extensive and involved a large part of the hemispheres and the vermis, and was not confined to the anterior part of the vermis, as in his case.

Cases of simple or serous cysts of the cerebellum have been described by Sharkey, Hadden, Habershon, Williamson[2] and others, and the origin of these cysts is obscure. The last mentioned writer lays stress on the importance of a thorough microscopical examination of the wall of such a cyst. In two cases of cerebellar cysts, after careful dissection and fairly complete microscopical examination, he failed to detect any evidence of tumor, and regarded them as simple cysts, but further examination revealed a small patch of new growth. In one case a minute oval glioma measuring only three-thirty-seconds of an inch by about three-sixteenths of an inch (about 2.5 mm. by 4 mm.) was found in the wall of a cyst nearly the size of a pigeon's egg, and in the other case a tumor (gliosarcoma four-sixteenths of an inch in diameter (6 mm.) was found in the wall of the cyst. Williamson thinks that if a tumor can undergo cystic degeneration to such an extent that only so small a portion remains as in the cases alluded to, it is not improbable that in some cases the whole of the growth may disappear and only a cyst remain. He does not deny that these cerebellar cysts may arise in some other manner, but in support of his opinion that they are degenerated tumors, he mentions that in cases in which they have been found the history and symptoms have been those cerebellar tumor, that cerebellar tumors are especially liable to undergo cystic degeneration, that simple serous cysts are exceedingly rare, and that minute tumor masses have been found in the walls of these cysts. Williamson does not entertain the view that the cyst may have formed first and the tumor later, and yet it seems to me this possibility should not be ignored, although in Case 1 of this paper it is probable that the glioma developed before the cyst. The wall of a congenital cyst may possibly be the starting point for a neoplasm, and a minute tumor found in the wall of such a cyst might possibly have developed into a large growth if death had not put a stop to the process. This view is strengthened by the recent report of a case by Schule.[1] A cyst was found in the vermis communicating with the fourth ventricle by a small opening about the size of a pea. The cyst-wall was lined with ventricular epithelium, and contained a sarcoma about the size of a pea. Schule believed this cyst was the persisting diverticulum of the fourth ventricle seen in lower animals, but never yet in mammalia, and he believed that the sarcoma developed in the wall of the congenital cyst after a trauma.

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[1] Leimbach. Deutsche Zeitschrift für Nervenheil-kunde, Vol. 1.

[2] R. T. Williamson, American Journal of the Medical Sciences, 1892, Vol. CIV, p. 151.

The tumor in Case 2 was round, about one inch in diameter, and was a fibroma. It had probably caused no symptoms, although it had considerably compressed one lateral lobe of the cerebellum. The lesions of amyotrophic lateral sclerosis were found by microscopical examination.

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[1] A. Schule Deutsche Zeitschrift für Nervenheilkunde. Vol. 18, p. 110.

The chief interest in these three cases lies in the presence of cerebellar lesions without cerebellar symptoms.

REMARKS BY DR. WM. E. ROBERTSON ON A CASE OF TUMOR OF THE CEREBELLUM AND ON A CASE OF TUMOR ON THE CORPORA QUADRIGEMINA.

Case 1.—CEREBELLAR TUMOR.—Mrs. Martha G., aged 37, married, mother of 9 children, one miscarriage.

Family History.—Father died of influenza. Mother living, has cardiac asthma. Four sisters living and healthy. No brothers.

Previous History.—She had been addicted to the use of alcohol for several years. Always healthy, never having an illness of any kind till she began to suffer severely with headache, about six years ago. The headache began after a confinement, the pain being at the base of the brain. She has had this pain from time to time ever since, always much more severely after a confinement. She has had two more children since the one born contemporaneously with the onset of the pain, six years ago. The last child was born July 29, 1900. The labor, like every preceding one, was normal. She was delivered by a midwife. Several days later, Dr. Saxman, to whom I am indebted for this history, was called, owing to the intense pain which the patient complained of as being located at the base of the brain. The pain was continuous, with acute exacerbations, during the next four weeks. Otherwise nothing abnormal was detected. She did not develop fever at any time, though she had a couple of chills, but no sweats. There had been no history of convulsions. She had no other evidence of renal insufficiency.

I made a careful inquiry in regard to cerebellar tumor in this case, and learned that there never had been any disturbance in the woman's gait. Apart from the inexplicable headaches she was considered a healthy woman, though, as I said, she was a potator, and this very likely explains the albuminuria which was detected. Her physician said he never had any occasion to have her eyes examined. She was not known to complain of vertigo at any time. She did have a fall a couple of years or more ago, but it may have been while she was intoxicated. She did not manifest any tendency to fall or stumble. She was admitted to the hospital in order that her condition might be studied carefully, as her social condition precluded the possibility of her receiving proper care at home. She had only been in the institution about fifteen minutes, when, with a thermometer in her mouth, she was suddenly seized with convulsions. These were general and very violent; they lasted about five minutes or possibly a little less, and she fell back dead.

Necropsy.—A few hours after death. Body of a very well-nourished woman, cyanotic; patechiæ on body surface. Breasts contained milk. Heart fatty, right auricle much engorged and dilated; small vegetations on mitral valve. Parenchymatous degeneration of kidneys and slight cirrhosis of liver. Every organ was intensely congested, actually dripping on section. Except for this and the conditions mentioned above they were all healthy. The uterus was enlarged, involution not having been completed, but presented no abnormality.

Brain.—Meninges congested. The only other abnormality being apparently a hemorrhagic area involving the vermis of the cerebellum and seemingly the posterior part of the fourth ventricle (due to an extension forward of what looked like a laminated membrane), as though hemorrhage had recurred from time to time, each time being followed by more or less organization of the effusion. The cord was not removed.

Cultures from spleen and kidneys negative. Cultures from the uterus showed a motile bacillus, coagulating and giving acid reaction with litmus milk (colon bacillus).

Case 2.—TUMOR ON THE CORPORA QUADRIGEMINA.—Sarah L., aged about 62, was admitted to the Episcopal Hospital, Harrison wing for chronic diseases, with a diagnosis of chronic rheumatism. At that time she was able to get about on crutches, but her joints were stiff, and her hands were deflected to the ulnar side, showing the chronicity of the trouble. Her mind was clear and, except as stated, she resembled any other woman of her years. Gradually some change in her gait was noticed and she became at first somewhat spastic. At this time sugar was present in her urine, although it almost disappeared under appropriate dietetic treatment. Soon a change in the character of her voice was noticed, and, shortly following, some difficulty in swallowing food. She often choked in swallowing. This was progressive and with it paralysis of all four extremities came on, so that she became totally helpless and eventually lost control of bladder and bowel. Death resulted from exhaustion superinduced by the inability to take food.

Necropsy.—Five hours after death. Body of a small woman. No lividity or rigidity. Subcutaneous fat well preserved.

Thoracic Cavity.—A few adhesions on both sides. No apical scars. Left lung crepitated throughout. Both lower lobes of the right lung were the seat of a croupous pneumonia. Heart small. Some thickening of all the valves and in the mitral and aortic valves some atheroma. Aorta dilated just above semilunar valves.

Abdominal Cavity.—Stomach fetal in type, retort-shaped and vertical. Liver small, much congested, cirrhotic and slightly fatty. Gall-bladder contained three large and two small stones. Common duct patulous. Spleen normal in size and consistency. Kidneys small and rather pale, firmer than normal. On section, cortex narrow; capsule strips with difficulty, tearing parenchyma. Pancreas apparently normal. Appendages and uterus normal.

Brain.—Meninges somewhat congested. There seemed also to be an excess of cerebrospinal fluid. Situated on the pons and between it and the cerebellum was a firm tumor about the size of a large marble. It was apparent only when the cerebellum had been removed. It had caused some depression of the cerebellum.

Cord.—Vessels enlarged and spinal fluid apparently increased.

REMARKS BY DR. WILLIAM S. WADSWORTH ON A CASE OF SCLEROSIS OF THE LEFT CEREBELLAR HEMISPHERE.

Case 3.—J. M., a strong, well-built white man of French descent. He had considered suicide for about three years, and spoken about it to a fellow-workman, to whom he said he had no reason for living, as his wife was no comfort to him. He was a sober, steady, capable workman, earning not less than $3 a day as an ironmolder, and had worked for nearly three years in the same place. He had no physical ailment that he complained of, beyond what he called bilious attacks. His work required strength, good eyesight and good co-ordination of muscles. He was quiet and kept by himself, being regular in his habits.

About three weeks before his death he was found unconscious in his room with the gas turned on, room closed and board-bill paid to that night.

He recovered under treatment and denied having attempted suicide, though he spoke about suicide to a fellow-workman afterwards. Later he was found unconscious in his room at about 11 o'clock and was taken to a hospital, where he was treated till 9 o'clock the same evening, at which time he died, having manifested the symptoms of opium poisoning.

POSTMORTEM NOTES.

Considerable lividity, especially of face; areas of reactionary inflammation (resulting from efforts of physician to keep the patient awake). Blood dark, fluid, as in asphyxia.

Brain.—Marked congestion of all vessels; slight edema. Left cerebellum quite firm, markedly reduced in size. Left vertebral artery smaller than right, not gaping, and having a scar as of an old local arteritis.

Lungs.—Marked edema and congestion; no serious lesions.

Heart.—Considerable congestion of vessels on surface of heart and aorta. Slight atheroma of aortic leaflets; at base some thickening.

Spleen, *Pancreas*, *suprarenals*, practically normal; *liver*, slightly hard and containing an area on the anterior surface, about ¼ x ⅓ x ¼ inch of hard, whitish scar-tissue, with some necrosis in centre; and another small area on under surface between the gall bladder and the left margin.

Stomach.—Slightly dilated; no marked pathological condition.

Kidneys.—Congested, rather soft, few small cysts on surface, otherwise in very fair condition.

Intestines.—Slight thickening of walls; areas of contraction.

Bladder.—Had been catheterized and considerable urine had been obtained, which was said to contain no albumin and no casts.

Extracted from The American Journal of the Medical Sciences, January, 1901.

ASTHENIC BULBAR PALSY.[1]

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AND

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(*From the William Pepper Clinical Laboratory, Phœbe A. Hearst Foundation.*)

We will give no historical account of asthenic bulbar palsy because Dr. Henry Campbell and Mr. Edwin Bramwell have only recently, in the summer number of *Brain*, published a careful summary of reported cases, and have made a thorough critical study of the literature. It will suffice to say that the first case was reported by Wilks in *Guy's Hospital Reports* in 1877. Wilks' patient was a stout, well-looking girl who could scarcely walk. The weakness seemed to be due rather to lethargy than to palsy. She spoke slowly, and had slight nystagmus. A month later many of the symptoms of bulbar palsy appeared, coming on rapidly in about three days. She spoke indistinctly, swallowed with difficulty, and was unable to cough. The limbs were not palsied. Soon breathing became difficult, and in a few hours she died. In the then state of knowledge it would have been proper to have expected to find organic bulbar disease. None was present. Careful macroscopical and microscopical examination revealed nothing abnormal. In 1879 Erb published a similar case, and from that time till 1886 nothing more was written upon the subject. About sixty cases have been reported, with twenty-three deaths and seventeen necropsies. These figures give a false impression of the death-rate, and the high percentage is due to the fact that neurologists are prone to report fatal cases, and many non-fatal cases are probably not diagnosed. At first it was thought the disease affected only muscles innervated from the bulb, but in recent years it has been found to be more wide-spread in bodily distribution, and now it is usually described under the title of myasthenia gravis.

For our own work we propose to relate a case that came to necropsy, to discuss another which, though resembling the first in many ways, yet differs enough to make its proper classification doubtful, and to speculate a little, for the matter is still speculative, as to causation.

We are indebted to Dr. Morris J. Lewis for the early history of the first case.

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[1] Read at the meeting of the College of Physicians of Philadelphia, November 7, 1900.

A woman, aged nineteen years, and married, came to the dispensary of the Infirmary for Nervous Diseases on April 26, 1899. Her family history was negative, her personal history unimportant, except that ever since her marriage, in 1897, she had had much trouble and grief—an unwished-for pregnancy and a brutal husband. In January, 1898, an abortion, probably induced, occurred. She felt no immediate serious ill effects, but about a year later began to suffer from numbness in the right hand, and later in the left hand, legs, and back. She could feel touch, pin-pricks, and the contact of objects without difficulty. The numbness was entirely subjective. Her condition remained the same until a few weeks before she came to the dispensary. She then rapidly grew weak in the arms and legs, so that she could not easily go up or down stairs, and sometimes fell when walking on a level surface.

Examination. She walked a little stiffly and as well with her eyes closed as open. Station was good. The pupils responded to light. The arms and legs were weak. The dynamometer registered fifty in either hand. The knee-jerks were exaggerated, quick, and equal. There was no ankle clonus. The elbow-jerk was exaggerated. She said she could not feel a sharp prick on the hands or legs, and only slightly on the face. She was, however, able to pick up a small piece of paper even when blindfolded. She could distinguish between hot and cold, but said she felt them but slightly. There was a slight tremor of the hands and head. The eyelids trembled and drooped somewhat, covering about half of the pupil. The lids did not come into close apposition on shutting the eyes. She could raise the lids, but not hold them up long. The tongue was tremulous, and when protruded turned toward the left. The respiration rate was twenty-six. The heart was normal. The sphincters were under complete control. There was slight contraction, but no reversal of the color fields. She was easily hypnotized.

She returned to the dispensary a few times, and then was lost sight of until her admission to Dr. Burr's wards at the Philadelphia Hospital on April 23, 1900.

Examination. A young woman of small frame, moderately well nourished, but somewhat pale. The head fell slightly forward upon the chest, and the eyelids drooped, partially covering the pupils. The face lacked expression. She could lift the head, but said it tired her very much to hold it up. She could not close the eyelids tightly, nor open them completely; there was but little power of movement in the frontal muscles, and she could not wrinkle the eyebrows. Her gait resembled that of a person convalescing from some serious acute disease. The movements of the arms were weak. There was no distinct palsy anywhere. Speech was slow and low-voiced—not aphasic, not paralytic, but simply weak. Mastication was slow, and she complained that eating tired her. Her whole manner and bearing showed languor and weariness, but that something more than mere neurasthenia was present was proven by the fact that the amount of weakness varied greatly in different groups of muscles, being most marked in those innervated from the bulb. The knee-jerks were large, but not spastic, and were easily exhausted. Neither ankle nor patella clonus was present. Babinski's reflex was absent; indeed, the plantar reflex was normal. There were slight but quite constant choreiform movements in the face and arms. There was no muscular atrophy of the lips, face, or tongue, and of course none in the extremities. She had difficulty in swallowing, solids seeming to stick in the throat and liquids making her cough. She still complained of numbness in the extremities, but felt touch, pain, and heat and cold well. Dr. Charles A. Oliver examined her eyes and reported: "Vision in each eye is reduced one-half to one-third, that of the right being slightly improved by pin-hole. Pupils are equal in size. Irides respond to light, accommodation and convergence. Extra-ocular movements are very much impeded, especially in outward direction, and more marked to the left. Palsy of convergence in association with a variety of ataxic movements. The eye-grounds are healthy, the fields of vision somewhat concentrically diminished. The patient is unable to close the lids, the action of the left orbicularis being more marked." Her condition remained the same until May 13th, when the difficulty in swallowing suddenly became very great, the temperature rose to 101° F., dyspnœa appeared, the pulse was rapid and weak, cyanosis and coma developed, and she died the next morning.

The necropsy was made the following day; it revealed nothing. The thoracic and abdominal organs were normal. There was a small calcified focus of tuberculosis at the apex of the left lung, and the spleen was chronically enlarged and its capsule much thickened. The kidneys and adrenals were not diseased in any way. The right ovary was cystic. The thymus gland was enlarged, but there was no other evidence of lymphatic diathesis. The uterus contained a three or four-months' old fœtus. The brain, after hardening in formalin, weighed 1250 grammes. Neither it nor the meninges showed any change on gross examination. The cerebrum was of full size, but the pons and medulla were distinctly smaller than normal. The pons was one-third less in diameter than others which had been hardened in the same way. The spinal cord was unusually broad in the lumbar region, and after removal of the dura showed a median dorsal fissure starting at the third lumbar segment and extending to the fifth. At first sight there appeared to be a distinct bifurcation of the cord, but section revealed a persistence of the posterior median fissure extending down to the commissure. The other regions of the cord were normal.

Microscopical Examination. Serial sections of the cord, medulla, pons, and floor of the third ventricle were stained by the Marchi, Nissl, Weigert, carmine, and nuclear stain methods. In the cord no pathological changes were found. In the medulla there were distinct chromotalytic changes with swelling and displacement of the nuclei in the cells of the upper nucleus of the tenth nerve (nucleus terminis vagi). The other bulbar nuclei, including the twelfth and nucleus ambiguous, were perfectly normal. We expected possibly to find changes in the seventh and third nuclei, but they were likewise normal. Sections of the cortex revealed no changes by any of the above-named methods. Sections from all the cranial nerves were examined. By the Marchi method black dots were seen scattered here and there throughout the twelfth, tenth, eighth, and fifth nerves; but inasmuch as similar appearances are seen in healthy nerves, or at least in nerves which have performed their functions well, we attribute no significance to them. Examination of the tenth nerve stained with carmine showed an atrophy of some of the nerve fibres, giving the appearance of a sclerosis. In the tenth and twelfth nerves some swollen axis-cylinders were seen. The muscles showed no pathological changes on microscopical examination.

There are two important questions in the study of this affection: Where is the disease located, and what is its nature? Morbid anatomy gives no help in answering these questions. In the larger number of necropsies no lesion at all has been found, and in the others the changes have been slight and indefinite, similar to those in our case, and of such a nature as not to prove, scarcely to suggest, that they had anything to do with the symptoms. We are compelled, therefore, to fall back upon general physiological and pathological laws, and to draw inferences from analogous affections. The disease must of course be seated in either the muscles or the motor neurons, and if in the latter it must affect either the upper motor neuron from the cerebral cortex to the bulb or cord, or the lower neuron from the bulb and cord to the periphery or some one part, cell body, or axon, of either. The symptoms are so predominately motor that there is no need to look for disease outside the motor apparatus. The disease has been thought to be muscular, but there is much evidence against it. In a large number of cases it has been found that on applying a tetanizing (faradic) current to the muscles at first a brisk contraction is produced, which gradually becomes feeble, and finally ceases, to reappear if the muscle is allowed a period of rest. With the galvanic current, on the contrary, no such exhaustion of muscular contractility occurs. Now faradism causes contraction essentially by acting through the nerves, galvanism by both the nervous system and the muscle directly. Further, Dr. Farquhar Buzzard, at the suggestion of Dr. Campbell, made the following experiment: A moderate galvanic current was applied to the biceps muscle, and a contraction obtained. The muscle was then faradized until it gave no response to a strong stimulus. Then it was tired out by making the patient flex the elbow against resistance, exerted until all power of flexion was lost. On applying the same strength of galvanic current as used at first an excellent contraction was obtained. Finally, on again applying the faradic current, the muscle was found to be still irresponsive. This experiment points strongly against disease of the muscle. Again, we know of no other affection due to disease of the muscles producing analogous symptoms, whereas organic disease of the bulb is not a little similar. Sudden death, a not infrequent thing in asthenic bulbar palsy, is not a symptom of muscular disease. There are several reasons for believing that the upper motor neuron is not affected. The myasthenic reaction, the exhaustibility of the knee-jerk, the pharyngeal palsy, the dyspnœa, the cardiac palpitation, all are evidence against cerebral disease. There is but little direct postmortem evidence in favor of the bulb as the seat of the disease. The slight changes that have been found were in it and in the cranial nerves. These changes, though almost certainly insufficient to cause the symptoms, may indicate the action of a toxin. The symptoms certainly point toward the bulb as the part first and most seriously affected. Considering everything we may say with comparative safety that the affection is one of the lower motor neurons, but whether the cell bodies or the axons are first and most affected cannot as yet be determined. The primary seat of disease may be in the motor muscular end-plates.

As to the nature of the disease but little is known. It looks like a toxin disease. It frequently follows some mycotic affection. It kills without visible wound. That poisons arising within or without the body may cause death without producing any discoverable lesion goes without saying. That there are diseases without a visible anatomical basis must be admitted, notwithstanding the dogma that there is never perversion of function without alteration of structure. In our case, as in a few others, we are inclined to believe that pregnancy had some causative influence. She was pregnant at the onset, and again when her disease became manifestly serious. Pregnancy may seriously disturb the normal metabolism of the body, as is shown in the kidney of pregnancy, the multiple neuritis occasionally seen, and the greater predisposition of pregnant women to certain diseases. Again, the smallness of the bulb may have had some influence. This was developmental, not secondary, not due to any acquired disease, not caused by the shrinking of an old sclerosis. What nervous elements were present were normal, but they were fewer than usual, they may have been dynamically weaker. It is possible that the ill-developed bulb was unable to withstand the stress of pregnancy.

The second case is made more difficult to understand by the presence of a singular type of anæsthesia. Sensory symptoms of any kind have been but little pronounced in the cases of asthenic bulbar palsy heretofore observed. Occasionally there is some little aching at the back of the neck and in the shoulders, with, it may be, numbness in the arms. True tactile anæsthesia has never been seen. In the case we are about to relate a very interesting form of anæsthesia was present, namely, asteriognosis, the inability to recognize objects by touch, though simple tactile sense is preserved. This symptom makes the proper classification of the case doubtful; but as it more closely resembles asthenic bulbar palsy than any other disease, we place it tentatively there. It would be interesting if in the future there should be met with cases of anæsthesia in the distribution of the sensory cranial nerves causing a condition comparable or at least analogous to the motor disease, bulbar palsy. This is a speculation, of course, but it is possible that such a condition may sometime be discovered. Our case then would be a connecting link. The history is as follows:

A young woman, aged twenty-four years, well educated and of excellent intelligence, with a good family and personal history, came to Dr. Burr, in March of this year, complaining of general neurasthenic symptoms and marked pseudo-emotionalism. She dated her illness from an attack of grippe which occurred in June, 1899. Whether this attack was one of influenza vera caused by the bacillus of Pfeiffer, or the so-called influenza nostras of unknown causation, could not be determined. At all events she never completely recovered. She was tired, languid, weak, and subject to spells of crying unaccompanied by any distressing emotional feeling. She did not regard her condition as serious, accepted no medical treatment, and grew steadily worse. A week before she came under observation her left arm began to be numb, and she had trouble in picking up small objects. A day or two later the numbness extended to the left leg, and still later to the right side. At the same time her neck felt somewhat stiff and there was severe pain in the occiput. She had slight vertigo, blurred vision, and occasional diplopia.

Examination revealed a spare, rather pale young woman. She was very emotional, bursting into tears without any cause. In the midst of her weeping she would say in the most matter-of-fact way that she did not know what she was crying about, and would go on talking about matters and things in general, paying but little attention to the lachrymal flood. Gait and station were normal; the knee-jerks were normal. Anæsthesia was absent. There was no deformity of the spine, nor pain on pressure anywhere in its length. Her condition was not regarded as serious. A week later, however, she suddenly developed palsy of the right face, involving the entire side. This was not an hysterical spasm, but a true palsy. A few hours later there came on excruciating pain in both ears, which lasted throughout the night, and required morphia for its relief. When re-examined there were found a little drooping of the eyelids, a little trouble in swallowing, slightly nasal voice, weakness of the muscles of mastication on both sides, but the right facial palsy had improved. On rising she would walk well for a few minutes, but soon would stagger and be compelled to sit down. All movements of the left arm were present, but all were weak, and soon she could not move the fingers or wrist against the slightest resistance. She could not squeeze the dynamometer at all. Power in the right arm and hand was a little greater. At no time was there complete loss of power in the arms. She could always make unresisted movements, but could not even lift a spoon, could not feed herself, and even unresisted movements soon tired her so much that she could not continue them. She could not write a word, could not grasp a pen strongly enough to hold it. In bed the movements of the legs were done weakly, but even at the worst she could stand and walk a little. The legs were never so seriously affected as the arms. She could move the tongue in all directions, but complained that the tip felt as if it had been burnt. There was no muscular wasting anywhere. The electrical reactions were normal, but unfortunately no examination was made for faradic exhaustibility. She had frequent attacks of pain in the occiput and back of the left ear, especially if she sat up in bed with the head unsupported. Palpation of the neck and head did not increase the pain at the time, but after an examination pain was apt to occur. No deformity of any kind was discoverable in the occipital region or in the cervical spine. There was no spasm of the muscles of the neck.

The knee-jerks were normal, and ankle clonus was not present. Touch, pain, and temperature-sense were normal on the arms, legs, and face; but later, when the power in the arms had returned and she could grasp well, it was discovered that she could not recognize objects by touch. This test, of course, could not be made while she was unable to handle objects. Smell and taste were normal throughout the course of the disease.

Dr. John T. Carpenter examined her eyes and reported as follows: "Central vision normal; field for form and color strictly normal. No reversal of the fields. No pathological changes in the eye-grounds. Refraction error; moderate hypermetropia. No diplopia except when red glass interposed, when vertical diplopia results and is constant. Right hyperphoria 2°, which is concomitant, not paretic. Ocular movements normal, though both adduction and abduction are below par (15°—5°). The only important factor elicited was the discovery of constant right hyperphoria." The sphincters were under complete control.

On first seeing the patient I did not regard her as seriously ill, but when the facial palsy appeared, followed by the difficulty in swallowing, the nasal speech, and the great muscular weakness, I began to fear a very serious issue, and believed that there was organic disease in the bulb and upper cervical cord or in the neighboring bones. Events proved this was an error, for after a few months she improved rapidly, and now is quite well.

There is no specific in the treatment of asthenic bulbar palsy. Rest is the most important element. The patient should be put to bed; faradism does harm; galvanism is of doubtful benefit; massage is useful. As to medicines, arsenic, in our experience, is the one drug which seems to be of benefit.

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THE RAPID DIAGNOSIS OF RABIES.[1]

BY MAZŸCK P. RAVENEL, M. D., AND D. J. McCARTHY, M. D.

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A rapid diagnosis of rabies is a matter of extreme importance for the physician and the patient, as well as for the general public. There is perhaps no other disease which strikes so much terror into the mind of the average person, and the cry of "mad dog" is a signal for general excitement. Any one bitten by a dog supposed to be rabid heretofore has been kept in a state of nervous suspense until it could be definitely determined whether or not the animal was a victim to hydrophobia. Up to the present time the only sure means of diagnosis in a vast majority of cases has been the inoculation of rabbits from a portion of the nervous system of the animal inflicting the bite; a practice often impossible to carry out with any degree of certainty, on account of the poor condition in which much material is collected. Even under the most favorable circumstances, from two to six weeks had to elapse before a positive diagnosis could be made. As well stated by Babes, it would seem "that this disease, so clearly characterized by a train of symptoms, constant in their character, ought also to present characteristic lesions in the nervous centres, and especially in the ganglia which preside over the production of symptoms," an opinion which has been generally accepted and acted upon by many students, their object being not only to disclose the cause of the striking symptoms, but also to find a method of diagnosis more rapid and more certain than any yet known.

The first step in this direction seems to have been due to Pollailon and Nepveu, who described the lesions observed in a man who had died of rabies. They noted that the whole cerebrospinal axis was strongly congested, and that the ganglion of Gasser was hyperemic and infiltrated with round or oval cells, some of them being hyaline in appearance, and which they considered "probably epithelioid cells from the capsule of the ganglion cells." The work of Balzer, calling attention to the changes in the central nervous system, was followed in 1874 and 1875 by Benedikt's article, both authors describing the distention of vessels in the nervous centres, accompanied by an extravasation of erythrocytes and leukocytes into the perivascular spaces. Kolesnikoff, in 1875, described besides, an invasion of the pericellular spaces by round cells occurring in the hemispheres, cerebellum, spinal cord and the sympathetic and intervertebral ganglia. Schaffer also made a careful study of the vascular and cellular changes found in the case of a man, and called attention to a hyaline and fibrillar degeneration and vacuolation of the cells of the anterior horns of the cord. In 1886 Babes concluded as a result of numerous researches, made in man and in dogs, both natural and experimental cases, that the essential lesion of rabies consisted in an accumulation of embryonic cells in the neighborhood of the central canal, and especially about the large modified cells of the motor centres of the bulb and cord. Writing again in 1892, Babes reaffirmed his observations and insisted on the profound changes taking place in the nerve cells. He held that it was possible to make a rapid diagnosis of the disease by a microscopic examination of the bulb and cord. He described in the bulb what he considered the diagnostic lesion of the disease, namely, the pericellular accumulations of embryonal cells described by Kolesnikoff, and for which he proposed the name "rabic tubercle." The cells of the bulbar nuclei undergo degeneration and present the various stages of chromotolysis. There is loss of the prolongations and a progressive modification and even total disappearance of the nuclei, a dilatation of the pericellular space, and an invasion not only of this space but also of the nerve cells by embryonal cells, and at the same time small corpuscles which are hyaline, brownish and in parts metachromatic. Many of the nerve cells become surrounded by a large zone of embryonal cells, and when the cell is completely degenerated these occupy the cell area and constitute the rabic tubercle.

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[1] Read before the Pathological Society of Philadelphia, January 10, 1901.

Since 1891 Babes has examined the bulb of 487 dogs, controlling his results always by inoculation of rabbits. His results have led him to trust this means of diagnosis and he still holds it to be one of the best means of rapid diagnosis at our disposal, although except in Babes' own laboratory the method does not seem to have been practised, at which he expresses a surprise which appears justifiable. Recently Nelis, working with Van Gehuchten, discovered in the spinal ganglia of two men who had died of rabies, and of a number of animals, peculiar changes which they considered to be the diagnostic lesion of the disease. They have confirmed all the lesions described by other authors, but in addition have noted what they consider to be more diagnostic than any other. The most profound, the most constant, and the earliest lesions are noted in the peripheral cerebral and sympathetic ganglia and the changes are especially marked in the intervertebral ganglia and in the plexiform ganglia of the pneumogastric nerve. Normally, these ganglia are composed of a supporting tissue holding in its meshes the nerve cells, each one of which is enclosed in an endothelial capsule (Fig. 1). The changes characteristic of rabies consist in the atrophy, the invasion, and the destruction of the nerve cells brought about by new-formed cells derived from the capsule, which appear between the cell body and its endothelial capsule. These new-formed cells increase in number, invade the protoplasm of the nerve cell, and finally completely occupy the entire capsule (Fig 2). These changes are widespread, but few capsules remain unaffected, and in advanced cases the section has very much the appearance of an alveolar sarcoma. The authors have considered in detail the findings of previous workers, but without exception they consider them as secondary and without any importance, either in the production of symptoms or in making a diagnosis. They hold that Babes has attached an undue importance to his rabic tubercle. In their first publication they held that "these lesions are specific of the rabic infection, if not by their nature, at least by their localization." In a later note, in answer to objections raised by Nocard and others, Van Gehuchten says that "the lesions of the cerebrospinal and sympathetic ganglia which he and Nelis have discovered are not specific of rabies in general; they are only specific of the disease as it occurs naturally." It is to be noted that the authors have made no claim regarding an early diagnosis of rabies, but only a rapid method. Van Gehuchten says his method "concerns not a precocious diagnosis, but only a rapid diagnosis in rabies." This has been further shown by

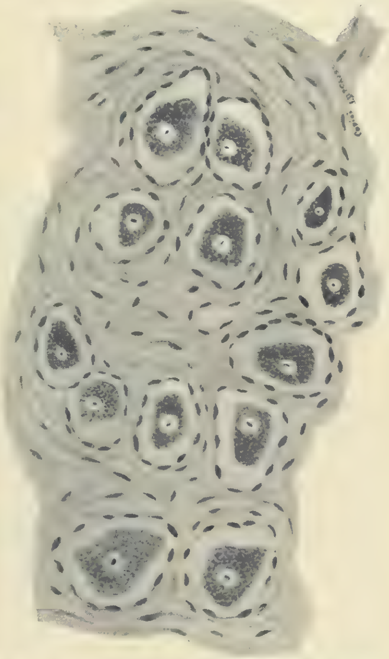


Fig. 1.—Normal Ganglion of Dog. (Reproduced from Crocq. Jnl. de Neurologie, V., No. 13.)

the experiments of Cüillé and Vallée, who, after inoculating dogs with the virus of rabies, sacrificed them at various times after the appearance of symptoms. They found that in animals in which the disease had just become manifest the lesions in the plexiform ganglion were slight or absent. They conclude that as a means of diagnosis the method of Van Gehuchten and Nelis has great value in the case of animals in which the disease has run its full course, ending in death.

The subject has been studied also by numerous veterinarians of note in Europe, notably Degive and Hébrandt of the State School at Cureghem, and Nocard and Vallée of France, all of whom have obtained results confirming the value of the discovery. Quite recently, Crocq has made a most thorough and complete review of the literature on the subject and a study of the method. He believes that Van Gehuchten is mistaken in considering the perivascular and pericellular neo-formations described by Kolesnikoff and Babes as unimportant changes and believes that by their constant character, their localization and evolution they have a considerable diagnostic value. He says: "The lesions described by Babes, and Van Gehuchten and Nelis, are both remarkable. They are so great and so clearly defined that I can understand how the authors, each on his side, may have concluded that the alterations described by them were specific." The procedure of Van Gehuchten and Nelis is, however, more simple and rapid than the method of Babes, and on this account is to be preferred. Our own work leads us to believe that the changes in the intervertebral ganglia are more constant than those in the bulb, as will be seen by reference to the summary below.

The method of procedure recommended by Van Gehuchten and Nelis is as follows: The ganglion is put at once into absolute alcohol, in which it is left for twelve hours, the alcohol being changed once. It is then transferred for one hour to a mixture of absolute alcohol and chloroform; next put for one hour in pure chloroform; then for one hour in a mixture of chloroform and paraffin, and lastly in pure paraffin for one hour. The sections are put in the oven for a few minutes, then passed through xylol, absolute alcohol and 90 per cent alcohol, after which they are stained for five minutes in methylene blue, according to Nissl's formula, differentiated in 90 per cent alcohol, dehydrated in absolute alcohol, and cleared in essence of cajuput and xylol. If frozen sections are cut they are put for a few minutes in 90 per cent or 94 per cent alcohol. In our work we have generally used 10 per cent formalin for fixing our tissues. They are then transferred to 95 per cent alcohol, and finally to absolute alcohol. For the most part the tissues have been cut without imbedding, being attached to blocks by the aid of mucilage of gum arabic, though in some cases celloidin has been used. For the bringing out of the chromatolytic changes the Nissl method has proved the best, but the capsular changes were best brought out in sections stained by hematoxylin and eosin. Since these latter changes are the most essential diagnostic features in the sections, we would suggest that material unfit for the Nissl method will still show the capsular changes when stained by hematoxylin and eosin.

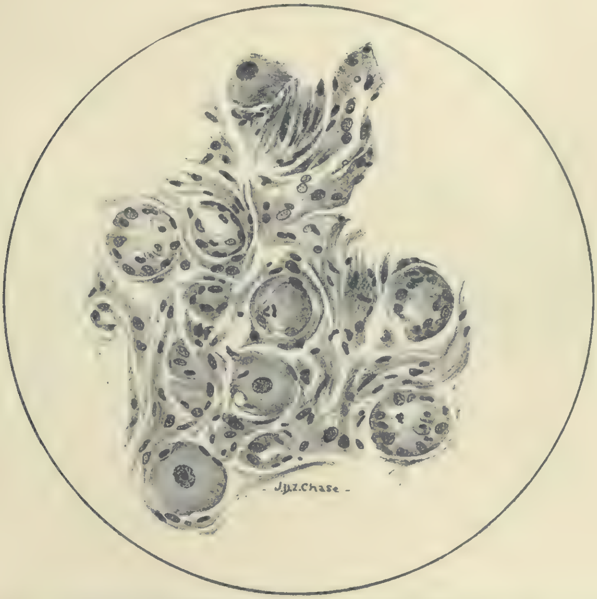
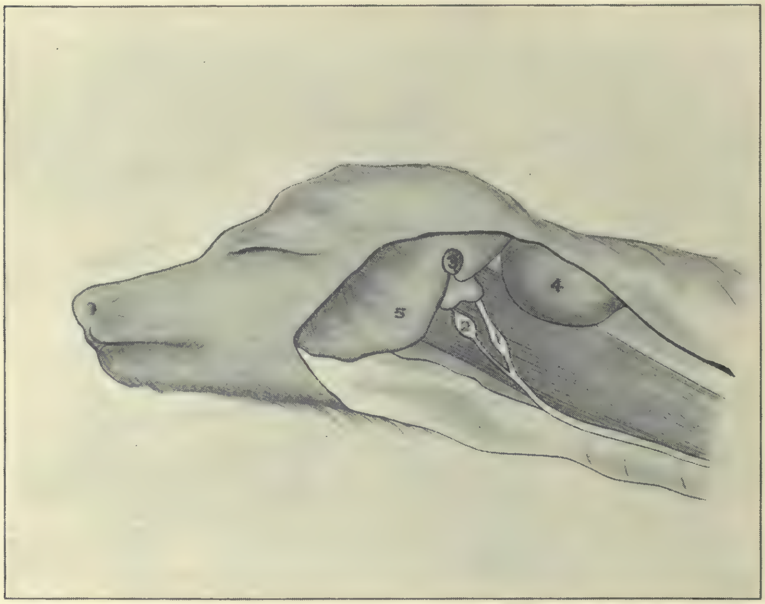


FIG. 2.—Plexiform Gangloin of Rabbit, dying of rabies produced by subdural inoculation. The capsules are filled or partially filled with foreign cells.

Up to the present time we have examined twenty-eight cases of rabies, including eleven dogs suffering with street rabies, one cow, one horse and fifteen rabbits, which were inoculated from these animals, a few being of the second generation, *i. e.*, inoculated from the first experimental animal. In all of the cases studied (twenty-eight), except that of the horse suspected of rabies, we obtained positive results in the plexiform ganglia. In one case, however, the changes were slight, and more marked in the peripheral (distal) portion of the ganglion. In twenty-one cases the bulb was examined for the rabic tubercle of Babes. Positive results were obtained in nineteen, though in two cases only chromatolysis, without distinct tubercle formation, was present. It will be seen that in two cases the rabic tubercle of Babes was not found, while the lesions described by Van Gehuchten and Nelis were present, though in one of these the changes in the ganglion were so slight as to leave us in some doubt. In this case, however, the subdural inoculation of rabbits gave positive results, and the microscopic examination of these rabbits showed the bulbar lesions of Babes as well as those of Van Gehuchten and Nelis in the ganglia. In the two cases mentioned in which the bulb showed only chromatolysis without distinct tubercle formation, the lesions in the ganglia were marked. One of these was the cow, which had shown clinical symptoms leading the veterinarian in attendance to suspect rabies. Two rabbits inoculated subdurally with the brain of this cow both died with typical signs of rabies, and by microscopic examination both the rabic tubercle of Babes and the lesions of Van Gehuchten and Nelis were found.



Dissection of Upper Cervical Region of Dog After Vallée. 1. Plexiform Ganglion. 2. Cervical Ganglion 3. External Auditory Meatus 4. Atlas. 5. Interior Maxilla.

Of the rabbits examined three had been inoculated with virus of the second generation from dogs having street rabies. One of these rabbits showed symptoms of the disease on the eleventh day after inoculation, the shortest time which elapsed in any of our cases between inoculation and the appearance of rabiform symptoms. The microscopic examination of these rabbits gave positive results.

Of the dogs examined six had shown unmistakable clinical signs of rabies, while five were only strongly suspected of the disease. All the cases were controlled by the inoculation of rabbits, except two dogs, in which the clinical symptoms left no doubt as to the diagnosis.

In the summary of our cases we have not included one which occurred in a human being for the reason that we obtained only a small portion of the upper cord, attached to which was a small fragment of an intervertebral ganglion, not observed until sections were examined under the microscope. In some of the sections a few ganglion cells were found which showed the typical proliferation of the endothelial cells of the capsule. Rabbits inoculated with the cord gave positive results, and some of these have been included.

We take this opportunity of putting this case on record. The patient was a girl eight years of age, who came under the care of Dr. Frederick Krauss, on August 12, 1900, by whom the diagnosis of rabies was made, and to whom we are indebted for the history. Six weeks before, the child had been bitten on the right ear by a stray dog which she was petting because it seemed to be sick. The dog was put out of the house and lost sight of. The wound was cauterized with nitrate of silver by a druggist, and healed without suppuration. On August 11 the child complained of lassitude, but was restless, and on account of these symptoms her mother gave her a dose of castor oil. The next morning inability to swallow was observed, being attributed to "sore throat." and soon after her mother noticed that, on being touched with a wet towel or exposed to slight draughts of air, she was frightened and startled. Dr. Krauss was called in on this day. The temperature was 100°, pulse 120. On giving her a glass of water she would look at it with dilated pupils for a moment, then suddenly grasp it and quickly attempt to swallow a mouthful. Every trial was followed by severe tonic convulsive contraction of the pharyngeal constrictors and the more external muscles of the neck, lasting about fifteen seconds. Repeated attempts were made, always with the same result. In reply to a question, she said that she was not afraid of the water, but it hurt her throat very much when she swallowed it. She shrank from the slightest current of air. Large doses of bromide of potassium and chloral with morphin were given, but without effect, and the symptoms grew more marked. She passed a sleepless night. On the morning of the thirteenth her temperature was 101.5°, pulse rapid. Later in the day she developed a state of intense excitement. She would lie quiet and apparently conscious for a time, then without warning suddenly spring up to her mother, crouch down with short cries of fear, looking at the wall with an expression of great dread, and seemingly unconscious of her surroundings. After about two minutes she would wake as from a dream. Repeated hypodermic injections of morphin had no effect, and she was sent to St. Christopher's Hospital. After a short remission the convulsive seizures became so frequent that almost constant inhalation of chloroform became necessary. When this was left off, she would utter short and loud cries of fear, which might well have been mistaken for the bark of a dog, and attempt to spring out of the bed. Death took place on the morning of the fourteenth, at six o'clock. The post-mortem examination revealed congestion of the brain and meninges and minute hemorrhages, while the severity of the convulsions was proven by rupture of the pleura. The train of symptoms left no doubt in the mind of the attending physician that the case was one of hydrophobia, and the diagnosis has been abundantly confirmed by the inoculation of rabbits, as well as by microscopic examination of the bulb and plexiform ganglia of these animals. The inoculations were carried through four generations, the rabbits all dying with typical symptoms of rabies, with the exception of one of the first generation, which died thirty-six hours after inoculation from septicemia. Besides the microscopic examination mentioned, full series of cultures were made, with the object of detecting any accidental infection during inoculation or after. These cultures remained sterile in every instance, so that we are able to exclude with certainty any known bacterial disease.

Our work has led us also to the study of a number of control cases which are as yet incomplete. So far as we have gone, however, they induce us to believe that the lesions described by Van Gehuchten and Nelis may, for all practical purposes, be regarded as specific of rabies. We bear in mind the opinion of Van Gehuchten himself, and held also by some other observers, that in dogs at least the changes in the cerebrospinal and sympathetic ganglia are only specific of the natural or street rabies. The lesions produced by the experimental inoculation of the " fixed " virus are not as marked as those in natural cases, and at times may be completely absent. We have not experimented with a fixed virus, but in rabbits inoculated with street virus of the first and second generations the gangliar changes have been marked. We have been convinced that the discovery of Van Gehuchten and Nelis is of great importance, from a scientific as well as a humanitarian standpoint. It can be rapidly and easily carried out, and should be a matter of routine in the examination of suspected cases of rabies in every laboratory.

In the examination of the medulla several sections were taken at random for mounting, but serial sections, extensive investigations of different portions of the bulb were not made, inasmuch as we were investigating rapid methods of diagnosis only, and not the essential nature nor the presence of these tubercles in the central nervous system. It is with this understanding that we recommend the examination of the ganglia rather than the bulb.

That these changes, or at least changes similar to them, might be expected in diseases where the intoxication is intense led us to inaugurate a series of experiments with tetanus and diphtheria toxins. In the mean time Crocq has reported his findings in the ganglia of a case of diphtheria, and since that time Spiller and Van Gehuchten have called attention to changes in three other cases, resembling those found in the ganglia in rabies. In Crocq's case the proliferation of capsular cells was present, but the absence of the perivascular changes, which are as diagnostic as the capsular changes, made the differentiation comparatively easy. In Spiller's first case, endothelioma of the Gasserian ganglion, the presence of the tumor mass causing the irritation leading to the capsular changes, and the slow course of the disease would lead to a correct conclusion. In the second case, one of meningomyelitis, the resemblance is very striking, but the capsular, interstitial and pericellular changes are of such an intensity as is hardly met with even in the dog and horse, where the changes are much more intense than in man.

The attention which the subject has attracted, and the large number of investigations which are being made in consequence, will probably lead to the discovery of isolated cases here and there in which lesions closely resembling, or perhaps identical with, those under discussion will be found. So far only four of such cases have been reported, all in man. While these are sufficient to make us doubt the absolute specificity of the lesion, it can be said with certainty that neither in man nor in any of the lower animals is there any condition known in which these changes appear constantly, except rabies. Their occurrence in this disease is so constant and so marked that we cannot but believe that they have great diagnostic value.

From our study of this subject the following conclusions seem justified:

I. When present, the capsular and cellular changes in the intervertebral ganglia, taken in connection with the clinical manifestations, afford a rapid and trustworthy means of diagnosis of rabies.

II. That when these changes are not present it does not necessarily imply that rabies is not present. The lesions afford contributory evidence more or less valuable, depending on the duration of the clinical manifestations.

III. That in certain cases when the capsular changes are slight, such as in animals dying or killed in the early stages of the disease, the changes are more marked in the distal-peripheral end of the ganglion.

IV. That the rabic tubercle of Babes is present sufficiently often to furnish valuable assistance in cases where only the central nervous system is obtainable without any of the ganglia, but in cases where the ganglia can be had they offer a simpler and easier method of diagnosis than do the brain or cord themselves.

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REMARKS ON THE IMPORTANCE OF THE SO-CALLED SPECIFIC LESIONS OF RABIES.[1]

BY WILLIAM G. SPILLER, M. D.

From the William Pepper Clinical Laboratory (Phœbe A. Hearst Foundation).

Much has been written in foreign languages on the lesions found in cases of rabies, and a careful review of the literature on this subject has been given recently by Crocq.[2] A few months ago a paper on the pathology of rabies was read before the Pathological Society of Philadelphia by Ravenel and McCarthy.[3] It is my intention to discuss briefly the importance of the lesions described by Babes, Van Gehuchten and Nelis, and others; and to show that these alterations are of diagnostic value, but are not confined to rabies.

Babes believed that the lesions of rabies consisted of an accumulation of embryonic cells about the central canal, and especially about the motor cell-bodies of the medulla oblongata and spinal cord. Perivascular cellular infiltration is common to many acute disorders of the central nervous system, but embryonic cells about the motor nerve cell-bodies have not been observed by Babes in other diseases than rabies. The rabic tubercles, as these collections of embryonic cells are named by Babes, are, according to him, the important lesions of rabies.

Van Gehuchten and Nelis say that the rabic tubercles are often absent in the spinal cord, but are present in the peripheral ganglia in cases of rabies, and here are formed by a proliferation of the endothelial cells of the capsules. Perivascular cellular accumulations also are found within the peripheral ganglia. These tubercles or nodules may become confluent, and when they do their origin is less distinct.

Van Gehuchten and Nelis, in two cases of rabies in man, found lesions in the medulla oblongata like those seen in acute inflammation, viz., dilation of the vessels, perivascular infiltration, hemorrhages and alteration of the nerve cell-bodies. These writers consider the changes observed within the spinal cord in rabies as of slight diagnostic value, but the rabic tubercles of the peripheral ganglia they at first regarded as specific. Babes, on the other hand, does not regard these lesions of the peripheral ganglia as of great importance. Crocq, after presenting fairly the two sides of the question, takes an intermediate position. The lesions described by Babes, as well as those described by Van Gehuchten and Nelis, according to Crocq's views, are of diagnostic value.

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[1] Read before the Pathological Society of Philadelphia, December 27, 1900.

[2] Cocq, *Journal de Neurologie*, July 5, 1900.

[3] Ravenel and McCarthy, Proceedings of the Pathological Society of Philadelphia, July 1900. New series. Vol. III, No. 9.

I shall not discuss the correctness of these opinions, but shall attempt to show that lesions similar to, and possibly identical with, those of rabies may occur in other conditions. I am indebted to Drs. Ravenel and McCarthy for their courtesy in placing before me for examination their carefully prepared specimens from cases of rabies.

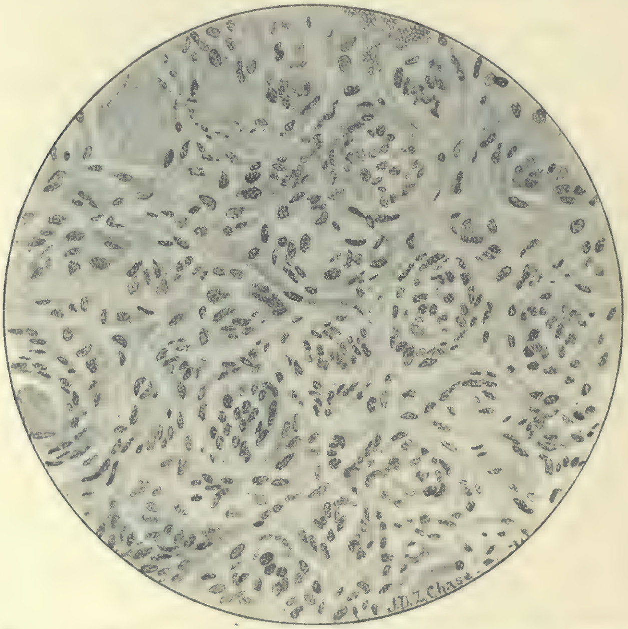

FIG. 1—A portion of the Gasserian ganglion in which the nerve cell-bodies have almost entirely disappeared. A concentric arrangement of the nuclei may be seen in different parts of the field, seeming to indicate that the cells of the capsule have proliferated and filled the spaces left by the destruction of the nerve cell-bodies.

Crocq (*l. c.*) examined peripheral ganglia from a child who had died from diphtheria, and found the rabic tubercles of Van Gehuchten and Nelis, but did not find the vascular lesions which are present in many cases of rabies. These findings of Crocq and, those of de Buck and de Moor, in a case in which death occurred from cancer of the rectum, induce Van Gehuchten[1] in a recent paper to acknowledge that the rabic tubercles in the peripheral ganglia are not specific, but are the result of a reaction following destruction of nerve cell-bodies from an intoxication of the organism. I know of no other reports by which it has been shown that the lesions of rabies are not confined to this disease.

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[1] Van Gehuchten, *Journal de Neurologie*, Nos. 19 and 20. 1900.

A study of some of the literature on rabies, in connection with my examination of pathological material from the nervous system, caused me to doubt whether the various lesions described in cases of rabies could be considered as specific to this disease. It seemed exceedingly improbable to me that rabies could cause lesions so different from those of other diseases, and it seemed more probable that the proliferation of the cells of the capsules within the peripheral ganglia was merely a result of irritation or intoxication. In my examination of the Gasserian ganglion in a case of endothelioma of this ganglion, reported with Drs. Dercum and Keen,[1] I found areas in which a proliferation of the endothelial cells of the capsule in the Gasserian ganglion, with complete destruction of the nerve cell-body, had occurred. These sections could not have been mistaken for those from cases of rabies, but they convinced me that from irritation, or intoxication, or some other cause, a tumor of this ganglion could produce a proliferation of the cells of the capsule about the nerve cell-body.

Another case from which I studied the brain and cord was sufficient to show that the lesions found in cases of rabies could occur in other diseases. This case was reported with Dr. Sherman,[2] and was one of acute ascending paralysis (Landry's paralysis), and terminated fatally in thirty-eight hours after the appearance of the first definite symptoms of motor disturbance. The symptoms bore some resemblance to those of the paralytic form of rabies, as in the latter also the paralysis is ascending. I found intense inflammation of the central nervous system and pronounced perivascular cellular infiltration. In the lumbar cord, where the nerve cell-bodies of the anterior horns had nearly disappeared, were accumulations of cells in the positions normally occupied by nerve cell-bodies. It was difficult to say positively that these accumulations were always about the nerve cell-bodies, as they concealed the latter if they were present. The condition was probably one called by Marinesco neuronophagia, to which attention has recently been called by de Buck and de Moor, and by Crocq,[3] *i. e.*, a destruction of nerve cells by round cells, probably derived from the neuroglia, and acting as phagocytes. I was able to find at least two nerve cell-bodies (Fig. 2, cells *a* and *b*) in one section from the lumbar cord, distinctly surrounded by round cells in the manner described by Babes as characteristic of rabies. The cellular infiltration of spinal ganglia from the lumbar region was intense, and in many places the proliferation of the endothelial cells of the capsules was distinct (Fig. 2), and in some areas these endothelial cells have replaced the nerve cell-bodies. Small hemorrhages and perivascular cellular infiltration were also present in these ganglia. In this case, in which no suspicion of rabies ever existed, I found the lesions described by Babes and those described by Van Gehuchten and Nelis, and they were more pronounced than in some cases of undoubted rabies. I therefore conclude that no lesions are specific to rabies, although under certain conditions the findings may be of considerable importance in the diagnosis of rabies.

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[1] Dercum, Keen and Spiller, *The Journal of the American Medical Association*, April 28, 1900.

[2] Sherman and Spiller, *The Philadelphia Medical Journal*, Nov. 31, 1900.

[3] de Buck and de Moor, *Journal de Neurologie*, March 14, 1900. Croqc, *idem*.

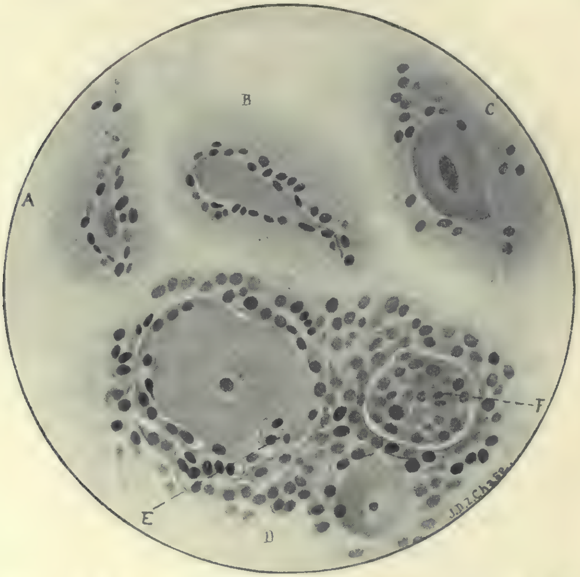

FIG. 2.—A, B and C nerve cell-bodies from the anterior horn of the lumbar cord, surrounded by round cells. D portion of a lumbar spinal ganglion. At E the proliferation of the cells of the capsule is shown. At F the nerve cell-body has entirely disappeared, and the cells of the capsule have proliferated and occupied its place.

ACUTE INTERNAL HYDROCEPHALUS. A CLINICAL AND PATHOLOGICAL STUDY.[1]

By CHARLES W. BURR, M. D.,

AND

D. J. McCARTHY, M. D.,

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PLATES XVII AND XVIII.

Clinical History.—W. S., male, white, 33 years old, was admitted to the Philadelphia Hospital on April 15, 1899, complaining of great headache, general weakness and abdominal pain. His family and personal histories were unimportant, possibly except that four years before he had had typhoid fever. On April 13 he stopped work, complaining of violent headache and pain in the back of the neck. The pain continued throughout the night, and the following day he became delirious and was sent to the hospital.

Examination showed a muscular man with flushed face. He lay in bed with the head retracted and the legs strongly flexed upon the abdomen. The temperature was 102° F., pulse 82, and respiration 24. He was stuporous but could be roused by sharp questioning. He would answer a few questions properly and would then become incoherent. Physical examination revealed no abdominal or thoracic disease. There were no palsies. The head was in extreme extension and could not be flexed. Lateral movement of the head was also impossible on account of muscular rigidity. Attempts at passive movement caused severe pain. There was no muscular rigidity elsewhere. Sensation, so far as could be determined, was normal. He was too weak to stand. The tongue was brown, the lips cracked and the abdomen distended. The plantar jerks and knee jerks were absent even with reinforcement. The bladder and rectum were under control. The urine contained a trace of albumin, a few hyaline casts, and had a specific gravity of 1027. The red blood corpuscles numbered 4,850,000, the white corpuscles 9000, and the hæmoglobin reached 75%. Widal's test was made repeatedly with negative results. Various culture media inoculated with blood remained sterile. The tentative diagnosis was acute meningitis.

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[1] **Read at the meeting of the Philadelphia Neurological Society, December, 1899.**

On April 22 Kernig's sign was present. Herpes of the lips and nose and a bluish mottling of the skin appeared. The mental state varied greatly. Sometimes the patient was restless and indeed quite violently delirious, at others stuporous, and again he would be almost normal, lying quiet, talking coherently and complaining only of headache and pain in the back of the neck. The pupils were dilated and slight lateral nystagmus was present. Slight deafness appeared. The plantar reflexes returned but the knee jerks remained absent. The eye grounds, examined by Dr. C. A. Oliver, were normal. On May 10 he was stone deaf. For several days he hiccoughed violently. The temperature which ever since his admission had been fluctuating between 101° and 103.4° F. now gradually dropped to normal and he improved greatly in all ways. Pain disappeared and the mind became clear and active. The knee jerks returned. Slight rigidity of the muscles of the neck persisted. His mental state was peculiar. He was perfectly coherent, could talk well and understood all that was said to him, but he was too well content with himself and his surroundings, he had no realization of his being sick and, though really too weak to stand, maintained that he was very well and would be out of doors in a day or two. He was trifling and jocose and, as his sister said, altogether unlike his usual self. He reminded one of a man in the beginning stage of paretic dementia. He gained greatly physically for a month and then the fever rose to 103° and the picture became the same as it was on admission. After a few days the fever again fell, and he again improved but for only a short time. On June 6 the temperature suddenly rose, the old symptoms returned, subsultus was added, nystagmus became marked and on June 9 he died.

Necropsy.—This was made the next day. The calvarium was normal. The dura was tense and elastic. The convolutions were broad, pale and flattened and the sulci were almost obliterated, appearing as lines beneath the pia. About the base over the cerebellum the pia was a little milky. The infundibulum was distended and pressed upon the optic nerves but not enough to distort them. On opening the ventricles a large amount of clear fluid escaped. All were dilated and the aqueduct of Sylvius was much wider than normal. The ependyma was boggy and separated easily from the underlying brain tissue. In the lateral ventricles it was roughened and at the tip of either inferior horn a band of white tissue stretched from the outer to the inner wall. The lining of the fourth ventricle was somewhat boggy. The choroid plexus of the third ventricle was injected and œdematous, that of the lateral ventricles was rolled up into an oval mass the size of a hazel nut and adhered to the walls. The spinal cord was very wet and in the lumbar region were several small hernia-like protrusions of the white matter into the pia. The dura was a little thickened in the cervical region. The heart and lungs were normal. The right pleura was adherent. The spleen was cirrhotic and the kidneys showed a subacute parenchymatous nephritis.

Histological Examination.—On microscopic examination the choroid plexus of the lateral ventricles showed a small tumor-like mass which on cross-section consisted of a capsule surrounding meshes of blood-vessels. There were a large number of hyaloid bodies (Plate XVII, Fig. 2, A, E, B), often twenty in one field, staining deeply with hæmatoxylin but taking only a faint stain with Lugol's solution. There was marked infiltration of small round cells in the capsule (Plate XVII, Fig. 2, C) and foci of them scattered through the sections. Their nuclei stained deeply and were about half the size of those of the ependymal cells. The vessels were distended with red corpuscles. The choroid plexus of the third ventricle showed similar but slighter changes; that of the fourth was normal.

The ependyma of the third ventricle showed microscopically the same tendency to separate from the underlying tissue as was noted in the gross specimen. A marked ependymal proliferation was present in the lateral ventricles (Plate XVII, Fig. 1). The nuclei of the cells varied in size, shape, and staining properties. The ventricular surface was covered by an amorphous granular layer several times thicker than the ependyma and containing nuclei scattered through it. A golden yellow pigment was present in the ependyma of all the ventricles. The vessels beneath the ependyma to a depth of one-half centimetre were actively congested and were surrounded by round cells (Plate XVII, Fig. 1, D). These cells not only occupied the perivascular spaces but also extended some distance into the surrounding tissue. The greater number of them were small round cells with nuclei slightly smaller than the nuclei of glia cells and surrounded by a narrow ring of cell substance. Though the nuclei of the glia cells within the area of infiltration were swollen and possibly proliferating we feel confident that the larger number of these cells did not arise from the glia. Scattered among the smaller nuclei larger, faintly-staining nuclei resembling very closely those of the endothelial cells of the capillaries were occasionally seen. They were probably endothelial in origin but of this there is no direct evidence. No polynucleated cells were present in the infiltration. Some of the large pale nuclei were irregular in outline but did not resemble the nuclei of polynuclear leucocytes in any other respect.

The neurogliar cells also showed proliferative changes. The nuclei of those immediately beneath the ependyma were at least twice the normal size and were surrounded by distinct cell bodies from which the processes radiated (spider cells). Further from the surface the nuclei became smaller, the protoplasm less, and the radiating processes finer until at a depth of about three quarters of a centimetre the tissue became normal. The area of change in the glia cells corresponded closely to that of congestion and round-cell infiltration.

The nature of the lesions suggested that they might have been caused by the reaction of the tissues to some toxic or irritative constituent of the ventricular fluid.

The cortical and spinal ganglion cells stained by Nissl's and Weigert's methods and by carmine showed nothing abnormal. The cranial nerves were stained by the Marchi method and carmine. The fourth and sixth showed a few black granules. The eighth pair were very much degenerated; the others normal. The spinal nerve roots showed only a few black granules in the lumbar posterior roots. The white matter of the cord showed no degeneration by the Marchi, Weigert, and carmine stains.

To sum up: A man is suddenly seized with fever, bradycardia, constipation, rigidity of the muscles of the neck, headache, stupor and delirium. After three weeks, during which the intensity of the symptoms varies greatly, he improves very much physically but shows many of the mental symptoms of paretic dementia. A week later fever and the meningeal symptoms return, last about a week, again intermit for four days only to return again and end in death. Post-mortem examination reveals only a moderate internal hydrocephalus, proliferation of the ependyma and ependymal glia, perivascular round-cell infiltration in the sub-ependymal tissues, and sclerotic and degenerative changes in the choroid plexus. What caused the lesions?

Internal hydrocephalus from mechanical causes is quite common, but idiopathic internal hydrocephalus is, or seems to be, rare and has attracted the attention of clinicians and pathologists only in recent years. Before the discovery of the tubercle bacillus it was quite common to call cases of hydrocephalus tubercular even though tubercles were not present. Barthez and Rilliet[2] separated these from those manifestly tubercular, but the credit of having established idiopathic internal hydrocephalus as a distinct clinical and pathological entity belongs to Quincke.[3] There are two varieties, one acute, the other chronic but often having acute exacerbations.

The acute variety is most frequent in children. In adults it usually follows injury to the head, the infectious fevers, especially typhoid and pneumonia, and acute or chronic alcoholic poisoning. The onset is sudden with headache, delirium, photophobia, vomiting and retraction of the head—symptoms resembling the irritative stage of septic or tubercular meningitis from which affections it may be impossible to differentiate it. Fever, however, may be absent or not so high as in septic meningitis and may either quickly disappear or vacillate with the other symptoms. The headache and muscular rigidity are not so intense nor so constant and the delirium, instead of persisting, alternates with periods of normal consciousness. The intermittency of the symptoms and the early increase of intracranial pressure, shown by choked disc, paralytic mydriasis, and, in early life, enlargement of the head, are characteristic. Examination of the cerebrospinal fluid is important. In tubercular meningitis the bacillus is often, although not always, present in the fluid withdrawn by lumbar puncture, and in septic meningitis inoculations of culture media give characteristic growths, and the fluid is either turbid or distinctly purulent and contains endothelial cells, leucocytes, red corpuscles, and pus microorganisms. In idiopathic hydrocephalus the fluid is under higher tension than normal, varying from 150 to 700 mm. (water manometer). It differs but slightly in its constituents from the normal, is clear and transparent, with a specific gravity of 1008 and contains albumin and sugar (?) in small quantities.

The chronic variety often follows the subsidence of the acute symptoms or, in children, may appear only with the increase in intracranial pressure caused by the union of the bones of the skull. A receding optic neuritis may be the only clinical manifestation. In other cases the symptoms may for a long time be vague and inconstant so that mere neurasthenia may be suspected. A large group present the symptoms of brain tumor. Optic neuritis is almost constant and transient or permanent bitemporal hemianopsia caused by varying pressure of the distended infundibulum on the optic chiasm may be present. Headache, vomiting, vertigo and local or general convulsions, and cranial nerve palsies are frequent. Localizing symptoms are almost never present except in the rare cases in which the hydrocephalus is confined almost entirely to the fourth ventricle and causes symptoms of cerebellar disease. The long course of the disease often ending favorably or seeming to do so only to recur, and the good effect of lumbar puncture point to the true nature of the disease, especially if the spinal fluid is found to be under high pressure at the time of puncture.

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[2] Barthez and Rilliet. Traité clinique et pratique des maladies des enfants. Paris, 1861.

[3] Quincke, Volkmann's *Samml. klin. Vortr.*, 1893, n. F., No. 67, and *Deutsche Zeitschr. f. Nervenheilk.* 1896, ix, p. 149.

Our case in the early stages was diagnosed as a meningitis of the convexity and of the cord. Typhoid and spotted fever were both thought of, but the continuous absence of the Widal reaction, the absence of spots, the non-enlargement of the spleen, and the clinical course excluded the former and the absence of eruption, of leucocytosis, of spinal-root symptoms, and the negative result of bacteriological investigation made the latter impossible. The peculiar variability of the symptoms, the afebrile intermissions, and the curious mental state made the diagnosis doubtful but it was retained as the best working hypothesis.

There are many points of clinical interest in the case. Kernig's sign which was at one time thought to be pathognomonic of meningitis was present during almost the whole course of the disease. The absence and subsequent return of the knee jerk and plantar reflex is also interesting. Absence of the knee jerk is not very uncommon in brain tumor but its return after an absence of three weeks without any lesion in the cord to explain it must be very rare. The absence could not have been caused by œdema of the cord because at autopsy that was very great though the reflex had returned several weeks before. We can only note the phenomenon, not explain it.

Central deafness with degeneration of both eighth nerves is not mentioned in any other case. It probably was caused by an unusual distribution of the pressure from the ventricles on the nerves at their exits. The optic nerves are most frequently affected and after them the sixth and seventh. In our case the optic nerves were normal save for a small focus of old degeneration near the centre.

The mental state may resemble paretic dementia. Indeed in Prince's[4] cases so close was the resemblance that that diagnosis was held for a time. Jocosity, a total neglect of the relative importance of things, and mild delusions of grandeur were the predominant factors in the mental attitude of our patient.

The pathological findings are interesting because in only a few of the cases heretofore reported have changes in the ependyma and subependymal tissues been described. Quincke[5] explains the absence of inflammatory changes in his cases by the subsidence of the primary hyperæmia subsequent to the occurrence of the hydrocephalus. The membranes of the brain may according to him be the seat of an acute serous inflammation like that which occurs in the pleura and the synovial linings of joints. In other cases the acute onset of the symptoms and their rapid disappearance make it seem probable to him that changes similar to those of angio-neurotic œdema may occur. In our case there were both recent and old changes in the choroid plexus. The proliferation of the interstitial tissue, the dilatation of the vessels, the round-cell infiltration, and the ependymal changes all pointed to an acute inflammation. The encapsulation of the plexus, the adhesions to the ventricular wall, and the bands across the tips of the ventricles indicated an old process. The large number of hyaloid bodies in the plexus of so young a man is evidence of degenerative change in the vessels leading to their obliteration and subsequent change into hyaloid material. All the steps in the process from hyaline degeneration of the media to complete obliteration, fragmentation, and calcification of the fragments are fairly well shown in the sections. That these bodies may have another and very different origin, namely, from proliferated endothelial cells blocking up the lymph spaces and undergoing hyaline degeneration, there is abundant evidence in the same sections, but the changes in the blood-vessels are the more important in connection with the other evidences of a chronic and acute inflammation in the plexus.

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[4] Prince. *Journal of Nervous and Mental Disease*, 1897, xxiv, p. 473.

[5] Op. cit.

The changes in the ependyma correspond to those in the choroid plexus. The thickened ependymal membrane and the adhesions and roughened surfaces of the lateral ventricles were of long standing. The acute inflammatory changes were widespread. Some authorities[6] hold that since the ependyma consists only of a layer of cells without blood-vessels it cannot be the seat of acute inflammation, but the distended network of capillaries immediately beneath the ependymal layer, the perivascular round-cell infiltration, the amorphous exudate on the surface and the hypertrophic changes in the glia must be considered to prove the inflammatory nature of the process. The fact that these changes were confined almost wholly to the ependyma and extended only a few millimetres beneath, gives the impression that they were the results of a local reaction of the cerebral tissues to some toxic action of the ventricular fluid rather than an acute primary inflammation leading to a serous exudation. To determine if possible which of these two conditions were present and to discover the effect of toxines and acids on the ependymal membranes we made the following experiments:

Sterilized urine, glycerine extract of the adrenals (P., D. & Co.), tuberculin, hydrochloric and carbolic acid were injected into the ventricles of kittens by means of a large hypodermic syringe.

The three adrenal kittens died within twenty-four hours. A slight increase of the nuclei surrounding the vessels immediately beneath the ependyma and dilatation of the capillaries of the brain substance for a short distance were the only changes noted. In one kitten there was intense dilatation of the vessels of the choroid plexus with hæmorrhages into its meshes.

Three kittens injected with urine were killed after three, six, and ten days. The changes were the same in all, differing only in intensity

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[6] Boenninghaus, Die Meningitis serosa acuta. Eine kritische Studie. Wiesbaden, 1897.

(Plate XVIII, Fig. 4). They consisted of a proliferation of the ependyma with an amorphous exudate upon the surface, swelling of the glia fibres which stained deeply, and a perivascular small round-cell infiltration, the whole resembling very much the condition found in the case here reported. In one specimen the layer of cells covering the choroid plexus failed to stain and looked very much like a fatty reticulum. In this specimen also a layer of round nuclei occupied the space immediately beneath the ependyma. Tuberculin gave similar but less marked results.

As dilute hydrochloric and carbolic acids produced the same effect we will describe the former only. The animals were killed at the end of a week. There was no excess of ventricular fluid. The ependyma looked normal and was not boggy or roughened. On microscopic examination (Plate XVIII, Fig. 3) the ependymal layer was intact, but the cells stained very faintly, the nuclei could hardly be seen, and the cell bodies were granular and their margins indistinct. Where this condition was most intense a granular layer covered the ependyma, evidently the debris of degenerated cells. Immediately beneath the ependyma and most marked on the under and inner surfaces of the ventricles a layer of round nucleated cells was present. They were four and five deep in certain areas and in others suddenly disappeared. They had small, round nuclei which stained deeply and were of the same size and character as those surrounding the deeper vessels. No polynuclear cells were found among them. Their probable origin was the network of capillary vessels beneath the ependyma. Columns of small nuclei surrounding the smaller vessels extended from this layer deeper into the brain substance. The glia network within the zone of capillary dilatation and perivascular infiltration was close meshed and had the appearance of a fibrillar structure running parallel to the ependymal surface. The columnar cells of the choroid villi were granular. The superficial cells were mere shadows and often the outer border was absent, making the surface of the plexus look frayed. The nuclei were either absent or only outlined and failed to stain. The condition appeared to be caused by a proliferation of the cells; the outer layer becoming degenerated and finally breaking down into an amorphous mass resting upon the surface of the other cells.

We conclude from these experiments that the non-purulent inflammation of the ependyma produced by acid irritants differs only in degree from the reactive changes following the injection of toxines into the ventricles. Changes in the ependyma without changes in the subjacent tissue probably do not occur. The inflammatory condition experimentally produced, by whatever agent, did not cause any increase in the ventricular fluid and the only evidence of an exudate from the ependyma was the amorphous material which probably was made up of degenerated cells.

The microscopic sections in the toxine experiments resembled the sections from the case reported and to that extent confirm the opinion that the changes found were secondary to a toxic condition of the ventricular fluid. The clinical history offers other evidence in support of this view. For example the mental condition of the patient, corresponding to that seen in other auto-intoxications, would be best explained by such an hypothesis. The exacerbations which Quincke compares in their sudden development and variability to angio-neurotic œdema appear to us to be rather the manifestations of varying intensity of auto-intoxication, such as occurs in uræmia and syphilis. Finally the hydrocephalus alone by its mere mechanical action, if sufficient fluid is present, can cause many symptoms.

DESCRIPTION OF PLATES XVII AND XVIII.

Plate XVII.

Fig. 1. Section of the floor of the lateral ventricle. Stained with hæmatoxylin-eosin. The marked irregularity of the floor is shown—caused partly by the folding of the ependyma (*C*), partly by the amorphous exudate on the surface (*B*), and partly by the hypertrophy of the sub-ependymal glia (*A*). The zone of perivascular small, round-cell infiltration (*D*) is seen extending some distance beneath the ventricular surface.

Fig. 2. Section of the choroid plexus of the lateral ventricle. *C*, the capsule very rich in nuclei. Hyaloid bodies in different stages are seen at *A*, where the hyaline change with calcification is beginning in a vessel, and at *B* and *E* has advanced to irregular hyaloid forms. The vessels of the plexus contain many leucocytes which are very rich in a granular pigment (*D*).

Plate XVIII.

Fig. 3. Showing the reactive changes in the ependyma and choroid plexus of a cat after the injection of hydrochloric acid (5%) into the ventricle. *A*. Granular degeneration of ependymal cells. *B*. Layer of round nuclei immediately beneath the ependyma. *C*. Perivascular infiltration of round cells extending deeper into the brain substance.

Fig. 4. Ventricular surface of the brain of a cat after injection of sterile urine. *A*. Granular degeneration of ependyma cells. *B*. Sub-ependymal layer of round nucleated cells. *C*. A vessel surrounded by an accumulation of round cells. The blood-vessels deeper in the tissue are not affected.

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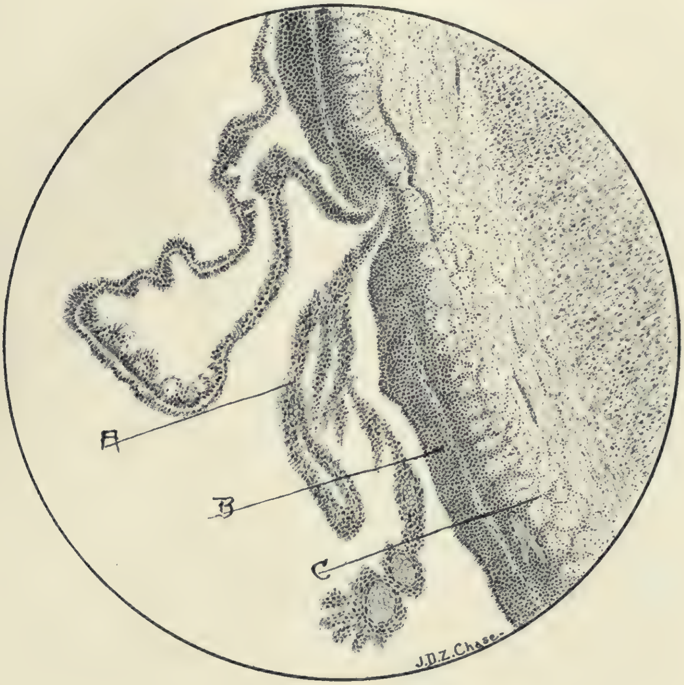

FIG. 3.

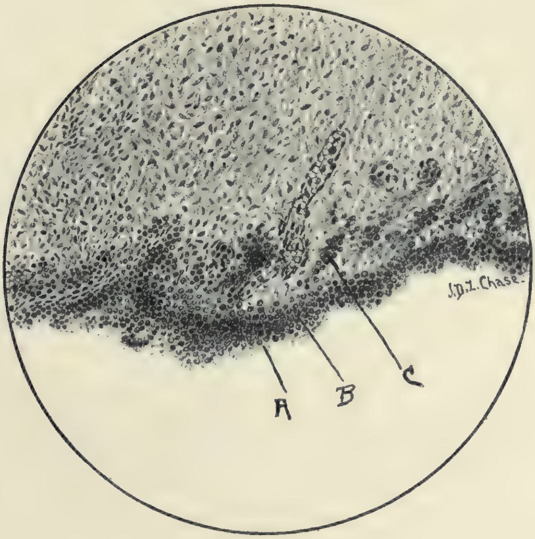

FIG. 4.

Reprinted from the *University Medical Magazine*, June, 1900.

OBSERVATIONS OF BLOOD CHANGES FOLLOWING CELIOTOMY.

By C. Y. White, M. D.,

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[From the William Pepper Laboratory of Clinical Medicine.]

The following studies of the blood in cases subjected to major gynecological operations were undertaken to determine whether the blood shows a reaction to these operations, and, if so, the relation ot these reactions to the course of convalescence. Prolonged etherization and the pathological lesions present (whether simple or suppurative, benign or malignant), have, to a certain extent, their expression in the blood. The post-operative changes in these conditions have been only partially studied, and it was the object of this work to elaborate previous studies in order to show the relation of these reactions to convalescence and the presence of reactions in possible complications that might arise during this period.

Corpuscular counts (Thoma Zeiss), estimations of hemoglobin (Fleischl) and coverglass spread preparations were made; the first of each of these, twenty-four hours before the operation, the second, within five hours after operation, and subsequently every twenty-four hours, until the patient's leukocytic count returned to normal or the patient had sufficiently recovered to make further estimation unnecessary, or, in a few cases, until they were unavoidably discontinued.

The coverglass spread preparations were kept until a suitable time, for further study, and then fixed by heat (brass plate) and stained with eosin and hematoxylon and Ehrlich's triacid mixture. The differential counts were made of 500 cells (eosin and hematoxylon stain) taken from two to five coverglasses. From the same specimens the general staining power of the erythrocytes and their general condition and degenerations were noted; and the same observations of the leukocytes were made. The latter were further studied with the Ehrlich triacid stain, so that in all 1,000 to 1,500 leukocytes were studied. The percentage of hemoglobin from day to day did not go hand in hand with the daily number of erythrocytes. In a few of the cases this difference was so slight that the usual errors of the Fleischl instrument and the Thoma Zeiss counter plus the individual error, and easily accounted for the irregularity; in other instances in which the inequality was well marked, it was undoubtedly due to a change in the blood, as repeated estimations gave the same results.

The erythrocytic count previous to operation showed in each of the cases a greater richness of the blood in these elements than would be expected from the general inspection of the patient and a knowledge of the clinical diagnosis and the duration of the illness; of the cases investigated, 14.8 per cent were acute and 85.2 were chronic. Another factor, which undoubtedly played a part in helping to give these high counts, was the preparation of the patient (during which preparation the first count was made), and the chief element of this is, as Hay has observed, the effect of purgatives, causing concentration of the blood. Even with this concentration of the blood there exists a secondary anemia of a slight grade.

The direct effect of the operation on the erythrocytic count, as estimated within the first five hours, was an increase in 34.6 per cent of the cases, a decrease in 53.8 per cent, while 11.5 per cent practically remained unchanged. Of the 34.6 per cent showing an increase, all had more or less excessive vomiting, which in a mechanical way and by the loss of fluid (the patients were allowed but a minimum of fluid for some hours) caused further concentration of the blood. In the 53.8 per cent that showed a decrease these factors were not so prominent.

In the succeeding counts many of the cases showed variations in the daily count. This was irregular in 26.9 per cent; a progressive decrease in 38.4 per cent; a progressive increase in 34.6 per cent. Where a sudden increase or decrease is marked, such factors as repeated vomiting, slight fever, frequent loose stools and a difference between the amount of fluids taken and the amount of urine voided, play an important rôle, and, in the great majority of cases, account for the sudden variation.

At the final count, the erythrocytes were found to have actually decreased in 62 per cent; increased in 23 per cent, and to have remained stationary in 15 per cent; but the changes were slight in favorable cases, so that they scarcely warrant consideration from a clinical standpoint.

The examination of the erythrocytes in stained specimens showed nothing, other than those changes ordinarily associated with the corresponding changes in counts; these were slight irregularity in size and shape, presence of some pale cells, absence of nucleated cells, polychromatophilia and basic degeneration. In Case 12 many very large cells—macrocytes—were seen; these appeared throughout the series and showed no change from the effects of the operation or the ether.

The study of the leukocytes of the blood in these cases offers the most distinctive features from a clinical standpoint, and may be divided: (1) The leukocytes in cases before operation; (2) post-operative leukocytosis; (3) the leukocytes in the complications occurring during convalescence.

1. The study of leukocytes of the blood in cases before operation may be subdivided into: (*a*) The leukocytes in cases in which there was inflammation and suppuration; (*b*) the leukocytes in cases in which neoplasms were present; (*c*) the leukocytes in cases in which there were present displaced organs.

In the cases in which there was inflammation alone, or inflammation with the presence of pus, 58.8 per cent showed the leukocytes to be within normal numbers (average 7,680), and 46.2 per cent showed a slight leukocytosis (average 13,383). Of these cases, 69.2 per cent were in a subacute or chronic stage, while 30.8 per cent were acute. Of those in the acute stage, Cases 7, 12 and 13 were within normal counts, while Case 14 showed only 10,440 leukocytes.

(*b*) Leukocytes in cases in which neoplasms were present (Cases 15–21 inc.). Three cases, or 42.8 per cent, were malignant, and four cases, or 57.2 per cent, benign. Of these seven cases three showed slight increase of leukocytes.

(*c*) Leukocytes, in cases in which there were present displaced organs (Cases 22–28 inc.). Backward displacements of the uterus gave no leukocytosis, while one case of prolapsed ovary gave 12.920, and Case 26, 10.840.

The differential counts in these cases before operation did not differ from counts of like pathological processes, under the same conditions in other parts of the body. The eosinophilia spoken of by Neusser and his pupils as occurring in diseases of the reproductive apparatus, especially of the ovary, was not found.

2. Post-operative leukocytosis. The cause of increase of leukocytes after operation must be due to a number of factors, and first among these is the effect of ether. Lerber, Schultz and Chadbourne found this increase to commence within a few minutes after the anesthetic was given, to increase for several hours and then to decrease until it reached normal limits, usually in two days. I have found this in four cases of pure etherization, and from this conclude, as did

Chadbourne, that the increase does not seem to depend upon the duration of the anesthesia, but upon the way the organism reacts to the drug. Besides ether, such factors as the incision into the abdominal wall, hemorrhage, the operative traumatism to the delicate structures within the peritoneum and the breaking up of adhesions certainly play a part in the causation of this leukocytosis. It is impossible to exclude any one of these causes; taken collectively they produce the post-operative leukocytosis. This was constantly seen in my cases. The highest count was recorded within five hours after the operation, excepting in severe case where glass drains were used (in these cases it was about thirty hours) and tended to fall to within normal limits in five days, excepting again in the cases where the glass drain was employed. In these cases it occurred several days later. A. E. Taylor has kindly given me the counts of twenty-two unpublished cases of celiotomies, in which he found similar results. The post-operative leukocytosis in Taylor's series averaged 19,500 cells; in my series 20,975.

The post-operative leukocytosis consisted of a relative and absolute increase of the polymorpho-nucleas neutrophiles, an absolute increase, at the expenses of the other cells, in 59.2 per cent; an absolute increase, with increase of the other cells as well in 25.9 per cent, an absolute increase with no change in the number of the other cells in 14.9 per cent of the cases. In other words there was an absolute increase of the polymorpho-nuclear neutrophiles in all the cases. The mononuclear cells increased in 40.7 per cent, decreased in 48.1 per cent and were not changed in number in 11.1 per cent of the cases. The transitional cells were increased in 55.6 per cent; decreased in 33.3 per cent, and remained unaffected in 11.1 per cent of the cases. The lymphocytes increased in 18.5 per cent; decreased in 70.3 per cent, and remained unaffected in 11.1 per cent of the cases directly following operation.

The eosinophiles disappeared in 96.3 per cent of the cases during the highest leukocytosis; in 3.7 per cent, or in one case, they remained, but in reduced numbers. They returned after several days, and after the leukocytosis had fallen considerably; their number was then decreased in 74.1 per cent, while 25.9 per cent of the cases showed a reappearance in appearently increased numbers.

3. The leukocytes in convalescence with associated complications. In this class have been included (1) local disturbances at the seat of the operation, as suggested by severe pain and tenderness, with eleva-

tions of temperature; (2) intercurrent affections—pneumonia, urticaria, stitch abscesses; (3) removal of drains; (4) secondary operations. These complications are to be found in Cases 1, 2, 3, 13, 15, 22 and 28. The complications had their expression in the blood in an absolute increase of the leukocytes, or a relative or absolute increase in the polymorpho-nuclear neutrophiles, or by a very sluggish fall in the total number of cells, as shown in the daily estimation.

Morphology of the Leukocytes.—The polymorpho-neuclear neutrophiles were of two types: (*a*) a large cell, with the granules well spread; and (*b*) a smaller cell with the granules densely packed together. In the former the nucleus stained poorly, while in the latter it was much more intensely stained. Often these cells were found side by side. In one case a few very small cells, about half the size of the usual cell, were noted.

The mononuclear and transitional cells showed nothing noteworthy; a few cells were very large and some few were vacuolated.

The lymphocytes were, as normally, of two sizes: (*a*) those with a small deeply staining nucleus, surrounded by a rim of protoplasm, often basic or slightly pinkish in color, and (*b*) a slightly larger cell, the nucleus not so intensely stained as in the former and having considerably more protoplasm, which was very slightly basic in character.

The eosinophiles and basophiles were normal.

Leukocytic shadows were frequently noted. Broken cells, surrounded by small granules staining pink with eosin and hematoxylon, were classified separately, until other specimens were stained with the Ehrlich triacid mixture, when these granules proved to be neutrophilic. The cells were then counted with the polymorpho-nuclear neutrophiles.

Summary.—The hemoglobin varied from day to day, and often without any relation to the erythrocytes.

Erythrocytes. These showed a higher count in the first estimation before operation than would be expected, considering the underlying conditions. After the operation, they showed an irregularity in the daily counts, and this in the majority of cases can be attributed to such factors as excessive vomiting, loose stools and a disproportion between the amount of urine voided in twenty-four hours and the amount of fluids taken. They showed no direct effect of the operation in their size, shape and staining qualities.

Leukocytes. The various pathological lesions in the pelvis produce no change other than those resulting from similar processes in other tissues. Post-operative leukocytosis is constant, and its height seems to depend on the severity of the operation. The highest counts were found within five hours after the operation, excepting in cases where glass drains were used, and then within thirty hours; the leukocytic count fell to within normal limits, on an average, in five days, excepting again in the glass drain cases, where the return to normal was slightly slower.

Complications during the course of convalescence had their expression in the blood in an absolute increase of the total leukocytic count, or in a relative or absolute increase of the polymorpho-nuclear neutrophiles, or in a sluggish fall of the total number in the daily estimation. In Case 2 count f. showed this change before other symptoms had developed.

The Value of Blood Examinations in such Cases.—Medical men as a rule are inclined to expect too much from blood examination, and especially from the leukocytic count, as recorded on the hospital charts or in their records; these counts are often made regardless of the stage of the disease, of complications of the disease, of the time of day, and of the medication, and are to a very great degree absolutely useless. Hubbard has attempted to show "the practical value of the blood count in surgical cases," by collecting hundreds of counts from the records of a large hospital, and comes to the conclusion, and rightly so, that such blood records are practically useless and of little value to the surgeon; but the condemnation lies not wholly in the blood counts, but in the attempts to make use of such records, many of which were taken under widely different circumstances.

The blood examination is a part only of a thorough examination of the patient, and should only be considered in connection with such examination. Undoubtedly a range of five to ten thousand leukocytes usually given as normal, is too wide a limit. Personally, I believe the normal number of leukocytes for an adult healthy person lies almost constantly in the neighborhood of seven thousand five hundred cells. Exceptions to this are undoubtedly found. Cases 10 and 23 probably show a much lower figure. In these the reaction following the operation was as constant as in the other cases, and the increase in percentage was about the same; yet a leukocytosis in the usual sense of the term cannot be said to be present, as they are within the range of ten thousand cells. The change in these cases can only be distinguished from the normal by the differential counts, and then only when the polymorpho-nuclear neutrophilic cells are above the average (see count b.), as above. Such changes suggest that we are dealing with a low normal number of leukocytes in this particular individual. Very often a second examination has to be made before anything of definite value can be learned from the counts.

This second count is of especial value in cases infected by the usual pus producing organisms. These infections as a rule give a leukocytosis when the process is acute and the patient is of average resistance, and do not give a leukocytosis when the infections are mild or very severe, with low resisting power on the part of the patient. In the latter instance the prognosis is grave. On the other hand, after the inflammatory process has been limited, or in the chronic cases where the primary focus has been thoroughly walled off, we find a stationary leukocytic count, or more frequently a falling count, or the count may be normal. Even in the latter instance the polymorphonuclear neutrophiles may show an increase, and be the only indication of infection. H. M. King, Cabot, and others also call attention to this fact. Cases do not occur, however, as Case 12, where marked evidences of an intense inflammation were present, and where the operation revealed a gangrenous perforated appendix, and yet the blood showed nothing indicative of such a change. This is the exception and not the rule, and its cause is probably to be sought in the nature or virulence of the infecting organism.

An elevation of temperature has in itself no great influence, except, perhaps, in so far as it may cause a slight concentration of the blood, but as fever is only a symptom of an underlaying condition, the blood changes are due to the primary trouble.

The Blood in Malignant Diseases.—In the early stages slight or no changes may be found ; later, the picture is a variable one, and finally in the last stages (stage of cachexia), we may have a profound secondary anemia, with or without a leukocytosis. Case 16 of the series illustrates a transitional stage of moderate severity.

(I am indebted to Professor Charles B. Penrose for the use of his wards ; to Dr. Henry D. Beyea for his help in selecting the cases and for their histories.)

TABLE I.

Date.	Case.	No. Count.	Hemoglobin. Per cent.	Erythrocytes.	Leukocytes.	Polymorphous nuclear.	Large Mononuclear.	Transitional.	Lymphocytes.	Eosinophiles.	Diagnosis and Notes.
Mch. 8.	**1**	a	65	4,400,000	12,640	78.6% 9,935	4.5% 569	4.3% 544	12.4% 1,567	0.2% 25	Tubal abscess.
Mch. 20.		b	65	4,460,000	17,720	86.6% 15,346	4.6% 815	1.8% 319	7.0% 1,241	. . . . . .	Celiotomy (exploratory). Extensive adhesions; fluids taken, ℥5; urine, ℥17.
Mch. 21.		c	67	4,401,000	17,040	78.9 13,445	2.3 392	2.8 477	16.0 2,726	. . . . . .	Fluids taken, ℥18; urine, ℥17.
Mch. 22.		d	70	4,110,000	14,840	70.0 10,388	2.9 430	4.1 609	22.5 3,339	0.5 74	
Mch. 24.		e	75	3,850,000	10,680	83.1 8,875	2.9 310	2.7 288	11.1 1,186	0.2 21	After opening abscess (trocar and canula) pus =Oj.
May 6.		f	61	4,330,000	11,440	68.9 7,882	2.5 286	3.6 412	24.6 2.814	0.4 46	Return to ward six weeks later, large abscess in the pelvis.
May 7.		g	60	. . . . .	21,440	90.6 19,425	2.5 536	1.4 300	5.5 1,179	. . . . . .	After opening and draining abscess per vagina.
May 8.		h	60	3,540,000	15,360	77.1 11,843	3.2 493	2.4 368	17.1 2,627	0.2 31	
April 8.	**2**	a	75	4,710,000	14,440	80.2 11,061	1.8 260	5.2 751	12.4 1,791	0.4 58	Tubo-ovarian abscess.
April 9.		b	75	4,300,000	26,520	87.0 23,072	4.2 1,114	2.4 636	6.4 1,697	. . . . . .	Celiotomy; removal of tubes and ovaries; intestinal adhesions; drain. Excessive vomiting; fluids taken, ℥16½; urine, ℥17; stools loose, 2.
April 10.		c	78	4,920,000	50,400	91.9 46,318	2.4 1,210	4.0 2,016	1.7 856	. . . . . .	
April 11.		d	80	5,120,000	44,880	90.7 40,706	2.3 1,032	5.0 2,244	2.0 898	. . . . . .	" " ℥19½; urine, ℥10.
April 12.		e	80	4,790,000	37,000	90.5 33,495	2.5 925	4.5 1,665	2.5 925	. . . . . .	Removal of drain; slight oozing of blood; hiccough; slight vomiting.
April 13.		f	78	5,190,000	24,800	91.7 22,593	3.2 794	3.4 843	2.3 570	. . . . . .	Suppuration of abdominal wound; fluids taken, ℥15; urine, ℥23; stools, 2.
April 14.		g	75	4,760,000	28,640	88.9 25,461	2.2 630	4.5 1,289	4.4 1,260	. . . . . .	Fluids taken, ℥12; urine, ℥27.

April 15 .		h	75	4,375,000	23,760	85.1 20,220	2.3 547	5.3 1,259	7.1 1,687	0.2 48	" " ℥25; " ℥19.
April 16 .		i	75	4,280,000	20,200	85.2 16,685	3.3 667	4.0 808	7.3 1,475	0.2 40	" " ℥31; " ℥26½.
April 21 .		j	68	4,350,000	17,680	74.6 13,189	3.1 548	8.7 1,538	12.7 2,246	0.9 160	
April 15 .	3	a	80	4,460,000	9,600	76.6 7,354	1.7 163	3.0 288	17.9 1,718	0.9 79	Tubo-ovarian abscess.
April 16 .		b	74	4,810,000	29,600	91.0 26,936	1.1 326	1.2 355	6.7 1,983	. . . . . .	Celiotomy, removal of tubes and ovaries; drain. Vomiting; flatus; fluids taken, ℥4½; urine. ℥10½.
April 17 .		c	80	4,710,000	18,280	89.2 16,123	1.2 219	2.3 421	7.2 1,316	. . . . . .	Slight pain in the abdomen; fluids taken, ℥17½; urine, ℥17.
April 18 .		d	78	4,590,000	14,200	79.3 11,317	3.9 554	3.2 454	12.5 1,775	0.7 99	Fluids taken, ℥33; urine, ℥17.
April 20 .		e	75	4,580,000	21,840	94.9 20,726	0.9 197	1.5 328	2.5 546	0.2 44	Shock; Pulmonary embolism; temp., 100.3°; pulse, 120; resp., 32.
April 21 .		f	73	4,700,000	22,880	90.1 20,684	2.0 458	2.5 572	5.1 1,167	. . . . . .	Fluids taken, ℥29; urine, ℥15; temp., 101°; pulse, 120; resp., 27.
April 22 .		g	. . .	. . . . . .	22,400	85.7 19,197	3.6 806	2.9 650	7.8 1,747	. . . . . .	" " ℥11; " ℥11; " 100°; " 120; " 27.
April 23 .		h	71	4,270,000	18,320	84.5 15,480	3.4 623	3.0 550	8.9 1,631	0.2 37	" 100°; " 127; " 27.
April 8 .	4	a	70	3,640,000	15,000	79.2 11,880	2.7 405	3.6 540	13.7 2,055	0.8 120	Salpingitis, ovarian abscess.
April 9 .		b	78	3,720,000	39,560	90.1 35,643	1.3 514	3.1 1,226	5.5 2,176	. . . . . .	Celiotomy—removal of tubes and ovaries. Adhesions; complains of severe pain in abdomen; temp., 101.3°; pulse, 110; resp., 24, 9 P. M.
April 10 .		c	74	4,080,000	28,240	85.6 24,173	4.1 1,158	2.8 791	7.1 2,005	0.4 113	Fluids taken, ℥6; urine, ℥17½; temp., 101.2°; pulse, 104; resp., 22, marked flatus, 8 P. M.
April 11 .		d	72	4,540,000	25,640	82.0 21,025	3.1 795	5.4 1,385	9.2 2,359	0.3 77	Fluids taken, ℥8½; urine, ℥17; temp., 101°; pulse, 96; resp., 26.
April 12 .		e	76	4,220,000	23,040	77.3 17,810	3.2 737	4.8 1,106	13.7 3,157	1.0 230	
April 13 .		f	76	3,840,000	19,520	67.2 13,117	6.6 1,288	4.9 957	18.5 3,611	2.8 547	

TABLE II.

Date.	Case.	No. Count.	Hemoglobin. Per cent.	Erythrocytes.	Leukocytes.	Polymorphous nuclear.	Large Mononuclear.	Transitional.	Lymphocytes.	Eosinophiles.	DIAGNOSIS AND NOTES.
Mch. 25.	**5**	a	67	4,460,000	12,460	82.5% 10.280	2.7% 336	4.9% 611	7.6% 947	2.3% 287	Pyosalpinx Bilateral.
Mch. 26.		b	67	4,410,000	36,040	95.1% 34,274	0.8% 288	1.5 541	2.6 937	. . . . . .	Celiotomy, removal of tubes and ovaries; drain. Fluids taken, ℥8; urine, ℥13½; slight vomiting.
Mch. 27.		c	55	3,400,000	33,080	90.6 29,971	1.6 529	4.1 1,356	3.7 1.224	. . . . . .	
Mch. 29.		d	43	2,650,000	16,080	80.0 12,864	0.9 145	5.4 868	13.7 2,203	. . . . . .	Removal of drain; fluids taken, ℥10; urine, ℥10.
April 15.	**6**	a	82	4,560,000	15,320	75.5 11,567	2.0 306	6.6 1,011	14.2 2,175	1.7 261	Pyosalpinx Bilateral; uterine fibroids.
April 16.		b	84	4,620,000	25,160	92.8 23,348	1.9 478	2.9 730	2.4 604	. . . . . .	Celiotomy; removal of tubes, ovaries, and uterus. Excessive vomiting; fluids taken, ℥5; urine, ℥12.
April 17.		c	80	4,450,000	17,880	83.3 14,894	2.1 375	4.9 876	9.7 1,735	. . . . . .	Fluids taken, ℥20; urine, ℥16; moderate vomiting, severe pain; temp., 100.3°; pulse, 80; resp., 20.
April 18.		d	78	4,530,000	19,160	81.6 15,635	3.8 728	6.0 1,149	8 6 1,648	. . . . . .	
April 19.		e	78	4,490,000	11,120	69.4 7,717	2.7 300	7.5 834	18.8 2,091	1.6 178	
July 15.		f	80	4,780,000	10,240	56.3 5,765	1.3 133	3.3 338	34.9 3,574	4.2 403	Returned to ward three months later.
July 16.		g	85	4,820,000	20,600	92.5 19,055	0.8 1,648	2.8 577	3.9 804	. . . . . .	Ether, removal of sutures in abdominal wall; slight vomiting.
July 17.		h	80	4,900,000	10,460	76.0 7,950	1.6 167	3.7 387	15.17 1,580	3.6 377	
April 29.	**7**	a	67	4,960,000	9,120	73.4 6,694	4.4 401	5.9 538	15.1 1,377	1.2 110	Pyosalpinx Bilateral, acute. Celiotomy; removal of tubes; drain (glass); temp., 100°; pulse, 110; resp., 24.
April 30.		b	67	4,970,000	13,440	83.4 11,209	1.8 242	2.8 376	11.8 1,586	0.2 27	Fluid from abdominal cavity, ℥2½; fluids taken, ℥2½; urine, ℥19½; slight vomiting.

May 1 .		c	75	4,930,000	16,160	84.7 13,688	3.5 566	4.9 792	6.7 1,083	0.2 32	Fluids taken, ℥26; urine, ℥20½; removal of drain tube; temp., 100.3°; pulse, 110; resp., 24.
May 2 .		d	85	4,730,000	13,120	85.9 11,270	2.1 276	3.6 472	8.1 1,063	0.3 39	Temp., 100°; pulse, 102; resp., 22.
May 6 .		e	83	4,135,000	9,440	75.1 7,089	3.6 340	4.9 463	13.8 1,303	2.6 245	Removal of drain.
May 6 .		f	80	3,980,000	9,120	78.4 7,213	2.6 239	4.4 405	14.0 1,288	0.6 55	Temp., 101.4°; pulse, 118; resp., 24.
April 22 .	**8**	a	84	5,040,000	8,640	60 6 5,236	2.3 199	3.1 268	29.2 2.523	4.8 415	Pyosalpinx and cystic ovaries.
April 23 .		b	81	5,040,000	27,040	94.9 25,661	0.6 162	2.1 568	2.4 685	. . . . . .	Celiotomy; removal of tubes and ovaries. Fluids taken, ℥6; urine, ℥19; excessive vomiting.
April 24 .		c	88	4,980,000	23,520	88.9 20,909	0.7 169	2.8 659	7.6 1,788	. . . . . .	Fluids taken, ℥14; urine, ℥14; excessive vomiting; temp., 100.1°; pulse, 70; resp., 18.
April 25 .		d	88	4,830,000	22,520	77.2 17,384	1.7 383	5.4 1,217	15.0 3.378	0.7 158	Complained of severe pain in the abdomen. Temp., 100°; pulse, 60; resp., 18.
April 26 .		e	76	4,670,000	10,400	65.0 6,760	2.9 302	4.3 447	24.9 2,590	2.9 302	
. . . .		f	. . .	. . . . .	8,400	60.5 5,082	1.9 160	3.7 311	30.4 2,554	3.5 294	
May 13 .	**9**	a	75	4,800,000	8,960	56.6 5,071	2.0 179	5.2 466	35.1 3,145	1.1 99	Salpingitis Bilateral; cystic ovaries.
May 14 .		b	83	4,550,000	19,560	92.9 18,171	0.7 137	2.5 489	3.9 763	. . . . . .	Celiotomy; removal of tubes and ovaries; radical cure for inguinal hernia, curettement. Fluids taken, ℥4; urine, ℥16.
May 15 .		c	85	4,790,000	19,760	86.1 17,134	1.8 358	4.4 876	7.7 1,533	. . . . . .	Fluids taken, ℥28; urine, ℥15.
May 16 .		d	80	4,890,000	11,280	82.5 9,306	1.9 214	4.5 508	11.1 1,252	. . . . . .	
May 17 .		e	75	4,280,000	8,280	69.3 5,738	2.7 224	6.3 522	20.5 1,697	1.2 99	
May 24 .	**10**	a	76	4,750,000	4,920	47.6 2,342	4.1 202	4.8 236	42.1 2,071	1.4 69	Salpingitis Bilateral; retroverted uterus.
May 25 .		b	74	4,560,000	11,160	90.2 10,066	1.7 190	2.3 257	5.8 647	. . . . . .	Celiotomy; removal of tubes. Fluids taken, ℥2½; urine, ℥13.
May 26 .		c	70	4,770,000	11,120	80.3 8,929	3.6 400	6.6 734	9.5 1,057	. . . . . .	Fluids taken, ℥30; urine, ℥21½.
May 27 .		d	72	4,720,000	9,620	72.0 6,926	4.4 423	6.6 635	16.0 1,539	1.0 96	

TABLE III.

Date.	Case.	No. Count.	Hemoglobin. Per cent.	Erythrocytes.	Leukocytes.	Polymorphous nuclear.	Large Mononuclear.	Transitional.	Lymphocytes.	Eosinophiles.	DIAGNOSIS AND NOTES.
April 23.	**11**	b	76	4,920,000	19,640	94.4% 18,540	1.5% 295	2.4% 471	1.7% 334	. . . . . .	Celiotomy; ruptured tubal abscess; abdomen filled with pus; drain (glass); temp., 100.2°; pulse, 152; resp., 30. Death.
Mch. 25.	**12**	a	53	3,390,000	6,640	56.8 3,772	1.8 120	5.4 359	33.7 2,237	2.3% 152	Appendicitis; acute gangrenous.
Mch. 26.		b	57	4,170,000	20,800	91.8 19,094	1.6 333	2.2 460	4.4 915	. . . . . .	Celiotomy; pus; posterior to cecum; drain. Fluids taken, ʒ8; urine, ℥18.
Mch. 27.		c	60	3,620,000	18,920	83.9 15,874	2.7 511	2.2 416	11.2 2,119	. . . . . .	Fluids taken, ℥23; urine, ℥14; temp., 101.3°; pulse. 100; resp., 22.
Mch. 29.		d	70	3,590,000	11,120	. . . *	. . . *	. . . *	. . . *	. . * . . .	Removal of drain.
April 22.	**13**	a	80	4,950,000	5,880	35.9 2,111	3.5 206	6.4 376	52.2 3,069	2.0 118	Appendicitis catarrhal.
April 23.		b	90	5,320,000	14,200	91.9 13,050	1.1 156	3.2 454	3.8 539	. . . . . .	Celiotomy; removal of appendix. Excessive vomiting.
April 24.		c	95	5,110,000	16,360	82.0 13,415	3.0 491	6.6 1,080	8.4 1,374	. . . . . .	Excessive vomiting; fluids taken, ℥4; urine, ℥14; temp., 100.4°; pulse, 90; resp., 22.
April 25.		d	95	4,570,000	12,120	83.0 10,059	2.5 303	4.8 582	9.7 1,176	. . . . . .	Slight vomiting; fluids taken, ℥13; urine, ℥16.
April 26.		e	93	4,900,000	8,120	70.7 5,741	2.7 219	5.9 479	20.5 1,665	0.2 16	
April 16.	**14**	a	77	4,740,000	10,440	74.1 7,736	2.7 282	6.5 679	15.4 1,608	1.3 136	Appendicitis catarrhal and pelvic hematoma.
April 16.		b	76	4,830,000	18,120	93.8 16,997	1.4 254	1.4 254	3.4 616	. . . . . .	Celiotomy; removal of tubes, ovaries, and appendix. Double drain. Fluids taken, ℥6; urine, 12.
April 17.		c	78	4,680,000	21,240	88.6 18,819	2.5 531	3.6 765	5.3 1.126	. . . . . .	Fluids taken, ℥24; urine, ℥14; temp., 100°; pulse, 112; resp., 36. A. M.
April 18.		d	75	4,130,000	18,520	86.1 15,946	2.9 537	3.2 593	7.8 1,445	. . . . . .	

Not estimated. *

TABLE IV.

Date.	Case.	No. Count.	Hemoglobin. Per cent.	Erythrocytes.	Leukocytes.	Polymorphous nuclear.	Large Mononuclear.	Transitional.	Lymphocytes.	Eosinophiles.	DIAGNOSIS AND NOTES.
Mch. 18 .	**15**	a	80	4,430,000	7,600	56.6% 4,302	5.1% 388	5.4% 410	30.8% 2,341	2.1% 160	Malignant adenoma of the fundus of the uterus.
Mch. 20 .		b	80	4,150,000	17,600	84.4 14,854	2.8 493	5.6 987	7.2 1,267	. . . . . .	Celiotomy; removal of uterus; drain per vagina. Temp., 100.4°; pulse, 104; resp., 26. Bloody discharge from vagina.
Mch. 21 .		c	85	4,190,000	19,480	85.5 16,714	1.3 253	4.3 838	8.6 1,675	. . . . . .	Fluids taken, ℥17; urine, ℥5; stools, 4. Bloody discharge from vagina.
Mch. 22 .		d	83	4,110,000	16,040	68.2 10,939	2.1 337	6.4 1,027	22.8 3,657	0.5 80	Bloody discharge from vagina.
Mch. 24 .		e	90	4,550,000	9,640	71.7 6,912	1.2 116	5.9 569	18.5 1,783	2.7 260	
Mch. 25 .	**16**	a	53	3,530,000	10,720	71.7 7,686	0.7 75	4.0 429	16.0 1,715	7.6 815	Malignant disease of the mesentery.
Mch. 26 .		b	50	3,115,000	20,200	91.9 18,564	2.2 444	1.6 320	4.1 808	0.3 61	Celiotomy (exploratory); removed blood cyst from omentum. Excessive vomiting; fluids taken, ℥4; urine, ℥11+.
Mch. 27 .		c	50	3,015,000	22,320	89.5 19,976	2.6 580	3.1 692	4.8 1,071	. . . . . .	Fluids taken, ℥3½; urine, ℥13; temp., 100.4°; pulse, 130; resp., 30.
Mch. 29 .		d	55	3,600,000	33,930	87.1 29,544	4.3 1,459	4.7 1,594	3.9 1,323	. . . . . .	Fluids taken, ℥35: urine, ℥17; temp., 102°; pulse, 142; resp., 28.
Mch. 30 .		e	53	3,600,000	24,360	87.5 21,315	1.5 365	3.9 950	6.91 1,68	0.2 49	
Mch. 31 .		f	47	2,870,000	20,920	89.7 18,765	2.1 439	3.5 732	4.0 837	0.7 147	
May 24 .	**17**	a	70	. . . . .	8,880	72.7 6,456	2.4 213	4.5 400	16.9 1,501	3.5 311	Malignant peritoneal papilloma.
May 25 .		b	68	5,450,000	12,560	86.5 10,864	1.9 239	3.6 452	8.0 1,005	. . . . . .	Celiotomy; too adherent to remove; drain (glass). Fluids taken, ℥5½; urine, ℥18; fluid from drain, ℥1.
May 26 .		c	64	5,430,000	13,280	84.0 11,155	2.2 292	4.5 598	9.2 1,222	0.1 13	Fluid taken, ℥43; urine, 17½; fluid from drain, ℥2½.
May 27 .		d	68	. . . . .	12,560	77.5 9,734	0.9 113	6.6 829	12.6 1,582	2.4 301	

April 1.	**18**	a	55	3,810,000	10,760	78.1 8,404	4.5 484	5.8 624	11.0 1,184	0.6 65	Multilocular papillomatous cyst; ascites; drain.
April 2.		b	45	3,360,000	16,400	93.3 15,301	1.7 279	2.2 361	2.8 459	. . . . . .	Celiotomy; removal of cyst. Adhesions to intestines; slight vomiting; fluids taken, ℥3½; urine, ℥23.
April 3.		c	43	3,510,000	11,560	92.7 10,716	0.9 104	2.9 335	3.3 382	0.2 23	Severe pain in abdomen; bloody discharge from vagina. fluids taken, ℥35; urine, ℥25; slight vomiting.
April 4.		d	47	3,310,000	10,840	83.6 9,062	2.7 293	3.7 401	9.3 1,008	0.7 76	Temp., 100.2°; pulse, 112; resp., 32. 3 A. M.
April 5.		e	. . .	. . . . .	9,480	77.8 7,631	1.8 171	3.2 303	13.6 1,289	0.9 85	
May 24.	**19**	a	70	4,720,000	8,600	68.6 5,900	2.5 215	4.1 353	20.4 1,754	4.4 379	Multilocular cyst of right ovary.
May 25.		b	76	5,640,000	18,120	90.8 16,453	0.2 36	1.3 236	7.5 1,359	0.2 36	Celiotomy; removal of cyst; drain. Excessive vomiting; fluids taken, ℥2½; urine, ℥13.
May 26.		c	80	5,750,000	20,160	84.4 17,015	2.1 423	4.6 928	8.9 1,794	. . . . . .	Slight vomiting; fluids taken, ℥30½; urine, ℥12; temp., 100°; pulse, 100; resp., 16. 2 P. M.
May 27.		d	73	4,950,000	19,600	83.2 16,307	6.2 1,215	3.6 706	6.2 1,215	0.8 157	Temp., 100.2°; pulse, 84; resp., 14. 8 P. M.
May 28.		e	71	4,870,000	12,800	81.6 10,445	3.0 384	4.3 550	9.7 1,242	1.4 179	
April 1.	**20**	a	65	4,540,000	8,960	55.4 4,964	6.4 573	4.8 430	29.5 2,643	3.9 350	Fibroids of uterus (multinodular).
April 2.		b	65	4,350,000	18,000	92.8 16,704	0.5 90	2.5 450	4.2 756	. . . . . .	Celiotomy; removal of tumor. Fluids taken, ℥3½; urine, ℥23; slight vomiting.
April 3.		c	63	4,420,000	15,440	85.5 13,201	2.7 417	6.8 587	7.8 1,204	0.2 31	Fluids taken, ℥23½; urine, ℥23; slight vomiting.
April 4.		d	63	4,250,000	14,960	84.1 12,581	2.4 359	2.4 359	11.1 1,661	. . . . . .	Fluids taken, ℥6; urine, ℥28; slight vomiting. Bloody discharge from vagina.
April 5.		e	. . .	. . . . .	11,240	77.4 8,700	3.7 416	4.7 528	12.6 1,416	1.6 180	
April 22.	**21**	a	55	4,120,000	10,400	67.3 6,999	2.8 291	5.1 530	24.6 2,559	0.2 21	Fibroids of uterus (multinodular).
April 23.		b	65	4,360,000	26,080	93.6 24,411	0.5 130	2.7 704	3.2 835	. . . . . .	Celiotomy; removal of tumor. Fluids taken, ℥4; urine, ℥13; excessive vomiting; severe pain in epigastrium.
April 24.		c	63	3,980,000	21,760	86.6 18,844	2.0 435	8.0 1,741	3.4 740	. . . . . .	Fluids taken, ℥13; urine, ℥18; temp., 101°; pulse, 98; resp., 24. Removed packing.
April 25.		d	60	4,370,000	27,160	84.2 22,869	3.0 815	7.9 2,146	4.9 1,331	. . . . . .	
April 26.		e	60	3,870,000	18,720	80.4 15,051	4.4 824	7.5 1,404	7.5 1,404	0.2 37	
April 27.		f	55	3,190,000	13,760	78.7 10,829	1.5 206	6.1 840	12.2 1,679	1.5 206	

TABLE V.

Date.	Case.	No. Count.	Hemoglobin. Per cent.	Erythrocytes.	Leukocytes.	Polymorphous nuclear.	Large Mononuclear.	Transitional.	Lymphocytes.	Eosinophiles.	Diagnosis and Notes.
June 4.	**22**	a	83	5,230,000	12,920	73.5% 9,496	2.1% 271	4.2% 543	19.9% 2,571	0.3% 39	Prolapse of ovary.
June 5.		b	84	4,860,000	31,680	85.4 27,055	2.7 855	3.4 1,077	8.5 2,693	. . . . . .	Celiotomy; removal of ovary. Fluids taken, ℥1; urine, ℥12; slight vomiting.
June 6.		c	83	4,870,000	15,520	83.8 13,006	1.3 202	6.8 10.55	8.1 1,257	. . . . . .	Fluids taken, ℥19: urine, ℥18½; pain in abdomen; temp., 100.3°; pulse, 102; resp., 22.
June 7.		d	76	4,660,000	13,880	85.5 11,867	1.1 153	4.2 583	9.2 1,277	. . . . . .	Fluids taken, ℥14; urine, ℥15; pain in abdomen.
June 8.		e	75	4,810,000	11,080	74.4 8.244	1.3 144	4.2 465	18.0 1,994	2.1 233	
Mch. 19.	**23**	a	95	4,600,000	4,885	71.5 3,493	4.1 200	4.3 210	19.8 967	0.3 15	Retroversion of uterus.
Mch. 20.		b	93	4,470,000	8,680	81.4 7,066	4.7 408	3.9 339	10.0 868	. . . . . .	Celiotomy; ventral suspension. Fluids taken, ℥3½; urine, ℥13; excessive vomiting.
Mch. 21.		c	93	4,530,000	6,880	78.8 5,421	3.8 261	5.8 399	11.6 798	. . . . . .	Fluids taken, ℥17½; urine, ℥18; severe pain in abdomen.
Mch. 22.		d	95	4,610,000	5,760	67.2 4.199	2.5 144	3.4 196	20.0 1,152	1.2 69	Fluids taken, ℥8; urine, 10.
Mch. 24.		e	93	4,570,000	5,240	66.7 3,621	2.7 141	6.7 357	19.8 1.038	1.7 89	
May 13.	**24**	a	71	4,970,000	7,240	73.5 5,321	5.0 362	3.7 268	17.0 1,231	0.8 58	Retroversion of uterus and mild cystitis.
May 14.		b	70	4,680,000	22,200	91.8 20,380	0.6 133	2.2 488	5.4 1,199	. . . . . .	Celiotomy; ventral suspension. Fluids taken, ℥1; urine, ℥18; excessive vomiting.
May 15.		c	77	4,640,000	15,680	84.6 13,265	1.9 298	3.4 533	10.1 1,584	. . . . . .	Fluids taken, ℥29; urine ℥19; slight sore throat and pain in chest; temp., 100°; pulse, 90; resp., 24.
May 16.		d	70	4,910,000	12,600	67.7 8,530	2.4 302	7.3 920	22.4 2,822	0.2 25	Temp., 100°; pulse, 100; resp., 24; pain in throat.
May 17.		e	70	4,960,000	9,000	73.4 6,606	1.8 162	8.5 765	16.1 1,449	0.2 18	Packing removed.

June 13 .	**25**	a	72	4,490,000	9,760	67.5 6,588	2.0 195	3.7 361	25.4 2,479	1.4 136	Retroflexion of the uterus and cystic ovary.
June 14 .			74	4,370,000	17,000	90.6 15,402	0.5 85	3.0 510	5.9 1,003	. . . . . .	Celiotomy ; ventral suspension ; curettement. Fluids taken, ℥3½ ; urine, ℥14.
June 15 .		c	70	4,295,000	11,720	77.9 9,130	2.3 270	4.0 469	15.4 1,805	0.4 47	Fluids taken, ℥32 ; urine, ℥24½.
April 8 .	**26**	a	75	4,520,000	10,840	75.6 8,195	3.4 369	5.1 553	15.5 1,680	0.4 43	Retroversion of uterus : lacerated cervix ; ruptured perineum.
April 9 .		b	80	4,640,000	21,120	91.7 19,367	0.9 190	4.6 972	2.8 591	. . . . . .	Celiotomy ; ventral suspension. Trachelorraphy perineorrhaphy. Fluids taken, ℥4 ; urine, ℥25.
April 10 .		c	78	4,320,000	16,760	85.5 14,330	4.2 703	4.4 738	5.9 989	. . . . . .	
April 11 .		d	80	5,450,000	12,720	8.04 10,227	4.4 560	7.8 992	7.0 890	0.4 51	Fluids taken, ℥13 ; urine, ℥15.
April 12 .		e	85	5,350,000	9,280	72.2 6,700	4.4 408	8.2 761	12.8 1,188	2.4 223	
April 1 .	**27**	a	78	4,520,000	9,440	60.5 5,711	6.5 614	4.2 396	26.1 2,464	2.7 255	Retroversion of uterus; ruptured perineum.
April 2 .		b	75	4,490,000	24,520	91.7 22,607	1.0 245	2.7 662	4.1 1,005	. . . . . .	Celiotomy ; ventral suspension ; curettement. Fluids taken, ℥23 ; urine, ℥13 ; slight vomiting ; temp., 102° ; pulse, 100 ; resp., 24.
April 3 .		c	83	4,590,000	13,080	80.8 10,569	2.7 353	4.6 602	11.7 1,530	0.2 26	Urticaria ; pain in abdomen. Fluids taken, ℥23 ; urine, ℥13.
April 4 .		d	83	4,670,000	13,960	75.8 10,582	2.6 362	4.9 684	15.9 2,220	0.8 112	Fluids taken, ℥10½ ; urine, ℥21 ; urticaria.
April 5 .		e	. . .	. . . . .	8,680	. . . *	. . . *	. . . *	. . . *	. . * . . .	
April 29 .	**28**	a	75	4,590,000	12,160	67.8 8,244	4.1 499	2.7 328	23.6 2,870	1.8 219	
May 30 .		b	76	4,530,000	23,520	78.0 18,346	1.7 400	3.7 870	15.2 3,575	1.4 329	Celiotomy (exploratory). Fluids taken, ℥22 ; urine, ℥24 ; excessive vomiting.
May 1 .		c	73	4,280,000	13,520	86.0 11,627	2.2 294	3.7 500	8.1 1,096	. . . . . .	Fluids taken, ℥22 ; urine, ℥21 ; pain in abdomen.
Arpil 2 .		d	75	4,360,000	10,640	74.2 7,895	2.0 213	7.3 777	16.0 1,702	0.5 53	

* Not estimated.

THE BLOOD IN INFANCY AND CHILDHOOD.*

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THE ERYTHROCYTES.—The red corpuscles are more numerous at birth than in the normal condition in after-life. The average of the enumerations of various investigators is 5,742,080 per c.mm. The counts obtained by these investigators are as follows:

Hayem	averaged	5,360,000
Sörensen	"	5,665,000
Otto	"	6,165,000
Bouchat and Dubrisay	"	4,300,000
Schiff (one case)	"	6,658,000
Gundobin	"	6,700,000
Elder and Hutchinson	"	5,346,560
Schwinge greatest at birth		

Certain attending conditions are supposed to influence the number of cells, thus according to Hayem and Helot it has been found than when the umbilical cord was not tied until its pulsations had ceased, a greater number of red corpuscles was found than in cases in which immediate ligation was practiced.

Elder and Hutchinson in comparing the new-born infant's blood with that of its mother found the former always richer in the number of corpuscles, the difference being as much as 350,000 to 500,000 per c.mm. Gundobin attributed this high count to concentration of the blood by loss of water through the lungs. Schiff found the same and further that the number of corpuscles decreased when the child was put to the breast. Elder and Hutchinson and Gundobin speak of the variations in the daily count, but do not attribute such variation to the usual physiological processes such as the influence of diet, and Gun-

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dobin suggests that it may be the result of some change in the chemical composition of the blood as a whole. The number of red corpuscles begins to fall after the second day and in one case in which Schiff estimated the number in the morning and evening during the first fifteen days of life, there was an irregular declension. The first day's count was 7,628,000; the last day's count was 4,565,600; and the average for the fifteen days was 5,828,465. This decrease in the number continues during the first year according to Schwinge and Gundobin and then there is an increase up to the eighth or twelfth year when the number becomes approximately that maintained until adult life. The count of the two sexes is approximately the same both before the fourteenth or fifteenth years and after the menopause, but in the intervening years the count in women is apt to be lower than that in men.

The red corpuscles during the first few days and at birth vary greatly in size. Hayem estimated the variations at from 3.25 μ. to 10.25 μ. and Loos found the size from 3.3. μ. to 10.3 μ. This irregularity in size has been observed by many others. Gundobin claims that the hemoglobin is more firmly attached to the cell stroma in the new-born infant and he also calls attention to the great number of small-sized corpuscles. In general, however, the histologists find no difference in the structure of the red corpuscles in infancy and in the adult.

THE HEMOGLOBIN.—This is increased at birth as Taylor, Morse, Elder and Hutchinson, Rotch, and others have shown, but it tends to decline rapidly in the first few days of life. Gundobin found the proportion of hemoglobin greater at birth than in adults or in infants after feeding had begun. Rieder's investigations showed an excess of 25 per cent. to 30 per cent. at birth.

SPECIFIC GRAVITY.—This usually varies as the percentage of hemoglobin varies, so that at birth the specific gravity is high and subsequently it declines. Monti found it 1060 at birth; Rotch 1065; Hotch and Schlessinger 1066; and Moelle 1060. E. Lloyd Jones noted that the specific gravity was highest at birth and at a minimum between the second week of life and the second year.

It has generally been observed that the specific gravity like the number of cells decreases after the first two days. Hoch and Schlessinger found figures between 1048 and 1052 up to two years of age and 1052 to 1056 from two to six years. The following figures will indicate the specific gravity at different periods.

Monti found the average	1057	at two to four weeks.
" " " "	1050	" twelve months.
" " " "	1052	" two to ten years.
Rotch " " "	1048-1051	up to two years.

The investigations of Monti, Rotch and Hoch and Schlessinger show that the specific gravity may be stationary for weeks or months at a time in healthy children. The variation, for example, in two healthy children studied by Hoch and Schlessinger was only .0025.

THE LEUCOCYTES.—The white blood corpuscles are greater in number at birth than in the adult blood, this excess in number constituting that which has been recognized as the physiological leukocytosis of the new-born. The following figures have been found by the authors quoted.

Rieder to be	15,500	10 minutes after birth.
Oransky " "	16,980	immediately after birth.
Cadet " "	19,480	" " "
Elder and Hutchinson to be	17,884	average in 12 cases at birth.

During the first forty-eight hours of life there is a still further increase in the number of leucocytes after which the number declines, though the count still remains higher during the first and second years, than that found in the blood of the adult. The following table shows figures obtained at various times after birth:

Schiff	24,000-36,000	in first 24 hours.
Oransky	20,980	20 hours.
"	31,680	next day.
Gieffer	18,000	24 hours.
Rieder	16,500	8 hours.
After the third day		
Rieder 1 case	8,700	3d day.
" 2 cases	10,500	5th day.
" 3 cases	13,600	4th day.
" 3 cases	12,200	5th day.

After the second year the number gradually declines to that found in adult blood and the percentage of the various forms of leukocytosis also becomes normal.

Physiological influences, such as diet and digestion, have about the same effect on the leucocytes in the infant as in the adult, that is to say, a digestive leukocytosis is observed. From the frequent feedings of the infant, however, this leukocytosis is practically constant as Taylor has pointed out, but Gundobin has observed an increase of from 2,000 to 4,000 in the number of leucocytes after feeding. The same author has observed that daily variations of temperature have no effect.

With regard to the variety of leucocytes it may be noted that the same kinds of cells are found as in the adult blood though the proportions of the several forms are different. The most striking peculiarity in the differential count is the increase in the number of lymphocytes and the more or less proportionate decrease in the polymorphonuclear cells.

Gundobin gives the following figures: Lymphocytes 50 per cent. to 66 per cent., polymorphonuclear 28 per cent. to 40 per cent. This indicates a three-fold proportion in the number of lymphocytes as compared with the adult, and a corresponding paucity of the polymorphonuclear cells amounting to about a half. The weight of the child apparently has no influence either on the total number of leucocytes or on the proportions of the different forms. If the child is increasing normally in weight, the numbers already alluded to occur, but when there is a cessation of the normal growth or a decrease in weight, variations in the number of leucocytes and in the relative proportions of the various types are apt to appear. Daily variations of temperature or artificial elevations of temperature amounting to 0.6 per cent. C. apparently have no influence on the number of leucocytes. (Gundobin.) C. S. Engel found 12 per cent. to 20 per cent. of polymorphonuclear cells in infants during the first few months of life and 40 per cent. to 50 per cent. after the expiration of the first few months up to the end of the first year. At twelve years of age he found 60 per cent. of polymorphonuclear cells.

The eosinophile cells vary greatly in number at birth and we find expressions as follows: "almost fail" (Elder and Hutchinson); "not increased" (Weiss); "in varying numbers" (Loos); "1.53 per cent. to 19.54 per cent." (Zappert); "often considerably increased" (Hoch and Schlessinger).

Nucleated red corpuscles are the embryonal type of the normal erythrocyte and, until the sixth month of intrauterine life, form the greatest number of the red cells of the blood. From this period until birth they gradually decline in number and at birth only a few erythroblasts can be found. By the end of the second day these as a rule disappear entirely. A few observers like Hoch and Schlessinger have found them in apparently healthy children. As a rule they are not found after the second or third day, excepting in children who are ill. Elder and Hutchinson found them as numerous as 1 to 20 and 1 to 8 of the leucocytes, in the blood taken from the umbilical cord. They also noted many free nuclei but no mytoses.

PATHOLOGICAL CONDITIONS OF THE BLOOD IN INFANCY.

The first changes observed in most cases of disease affecting the blood is a reduction in the hemoglobin and in the number of the erythrocytes, but as a rule the reduction in coloring matter is greater than that of the number of cells, especially in young infants and early childhood. No other change may be observed in the red cells, but on the other hand, there are often changes in size and shape. In the blood of infants Gundobin calls attention to the occurrence of the smaller forms, the so-called microcytes. A condition of the red corpuscles that has been commonly regarded as degenerative is its peculiar reaction to stains as a result of which the red cell becomes dichromatophilic or polychromatophilic. Loos has called attention to the microcytes and macrocytes as showing this change in particular, and the same author calls attention to the fact that the biconcavities of the same cells are usually lost, showing a change in the structure as well as in the staining properties of the cells. A still further change in these cells causes an increased adhesiveness so that they stick to the cover glass firmly. Loos' attention was first directed to this by observing that in specimens insufficiently fixed these cells and the leucocytes were the only ones to remain after washing the slides for mounting. The polychromatophilic change is a rather common one, being found in posthemorrhagic conditions and in most of the anemias. There is much difference of opinion as to the real cause or actual change in the cell. Ehrlich supposed that it was an evidence of senility or of death of the cells while Gabritschewski, Askanazy, Dunin and others opposed this theory and state that they have found it in young cells, *e.g.* around the nucleus of the megaloblasts. Basic or granular degeneration of the red corpuscles has not received the attention of investigators in the blood of children. Loos found cells with fine granules which he supposed to be the remains of a former nucleus and Ehrlich suggests that this change is a coagulation necrosis of the cell contents or that the granules are the remains of a former nucleus.

Nucleated red corpuscles: Erythroblasts. When these cells are found in the circulating blood after the second or third day of life, their presence may usually be assumed to indicate a pathological change or condition. The significance of erythroblasts is, however, much less in infancy and childhood than in the adult since marked anemia occurs so much more readily in early life. The number of the erythroblasts varies greatly at different times in the same patient and in like grades of intensity of a similar disorder in different patients. Erythroblasts have been found in secondary and in primary anemias by Weis, Gundobin, Elder and Hutchinson, Morse, C. S. Engel, Monti, Berggrun, Hoch and Schlessinger. Loos found them very abundant in pseudoleukemia, syphilis, rickets, osteomyelitis, congenital rickets and tuberculosis, and in less number in the same affections in slighter grades. Most investigators have found these cells under similar conditions. Karyokinetic figures are rarely found in the circulating blood and only in cases of very severe anemia.

Leucocytes. Increase in the number of leucocytes (leukocytosis) more frequently presents itself in the blood of anemic children than in adults and the increase may reach enormous proportions in apparently slight pathological conditions. The causes of leukocytosis in childhood are in general the same as those which occasion the condition in adults. We may distinguish toxic, inflammatory, posthemorrhagic, and cachetic forms. Enlargement of the spleen may or may not accompany the leukocytosis; in the majority of cases there is enlargement. The differential count of the leucocytes shows an increase in the lymphocytes, the mononuclear cells or the polymorphonuclear neutrophiles. The eosinophiles seem to be governed by influences quite different from those which control the number of the other forms, but the nature of those influences is as yet unknown. Myelocytes are more frequently found in the blood in childhood than in adults. Their occurrence in increasing numbers is of bad prognostic significance as C. S. Engel, Cabot, and others have especially noted in pneumonia and diphtheria.

We may now proceed to the consideration of the hematologic features of various general and local diseases.

INFECTIOUS DISEASES.—During the attack there is often but little change in the number of red corpuscles and the percentage of hemoglobin, while during convalescence a moderate or severe grade of anemia presents itself. This is explained by the assumption that the blood is inspissated in the febrile stage of the disease by increased action of the skin and lungs or by diarrhea. When anemia develops, the reduction in hemoglobin usually exceeds that of the number of corpuscles, and at times this disproportion is marked. The number of leucocytes differs in various diseases, being increased in some, and unaffected or decreased in others. Among those in which a decrease (or at least no leukocytosis) is observed, are rötheln, variola in its earlier stages (Pick), mumps (Cabot), influenza, malaria, typhoid fever, tuberculosis (before excavation and in miliary tuberculosis), and varicella (Loos and Engel). Very slight causes may determine a moderate leukocytosis in any of these as in healthy children. In other infectious processes and in those above named when complicated by inflammatory or other conditions considerable and often excessive leukocytosis may be met with.

With regard to the variety of cells mainly involved in such infectious leukocytosis, Weiss and Gundobin found the polymorphonuclear cells especially increased in diphtheria, scarlatina, erysipelas and pneumonia. Gundobin in addition found that the increase of the leucocytes occurred some time before the eruption in scarlet fever, measles and erysipelas. C. S. Engel found 67 per cent. of polymorphonuclear elements and no eosinophiles in varicella and three days later, when the skin lesions had healed, only 47 per cent. of polymorphonuclear cells and as many as 16 per cent. of eosinophiles. In measles Weiss failed to find increase of eosinophiles. In typhoid fever the number of leucocytes is decreased in childhood as in adults, and there may be at the same time a decrease of the hemoglobin and the red corpuscles. The number of leucocytes is relatively increased or properly speaking the polymorphonuclear elements are the ones actually deficient, the mononuclear cells, large and small, being present in about the normal number.

The hematological conditions in *pneumonia* are particularly interesting. There is nearly always some degree of leukocytosis and often excessive grades. When the condition is absent, the prognosis is unfavorable in childhood as in adults. Gundobin found in six cases an average leucocytic count of 24,300 with the following differential count: lymphocytes 25 per cent., mononuclear, 6 per cent., polymorphonuclear 70 per cent., eosinophiles 2.5 per cent. Engel found the polymorphonuclear cells excessive and the eosinophiles wanting during the febrile period of the disease, the latter forms reappearing after the crisis. Rotch found that leukocytosis develops at from six to twelve hours before physical signs are discoverable, and that a leucocytic crisis may antedate the crisis of temperature by twenty-four hours. A blood lysis is, however, more common.

In *hereditary syphilis* there is a more or less pronounced grade of anemia according to the severity of the symptoms. Usually the anemia is quite marked. In a careful study of the subject, in which Gundobin, Weiss, Monti and Berggrun, Bieganski and Engel are quoted, Loos arrives at the following conclusions:

1. Hereditary syphilis is accompanied by an anemia which under certain conditions may become very great.

2. The anemia is characterized by a decrease of erythrocytes with great degenerative changes (poikilocytosis) and especially the occurrence of microcytes and macrocytes, by the presence of polychromatophilia and nucleated erythrocytes which may be very numerous at times.

3. A leukocytosis at times reaching very high grades and showing a predominence of the small lymphocytes is usually seen.

4. The presence of myelocytes is noted.

5. Hemoglobin greatly decreased.

These changes indicate nothing that may be regarded as peculiar to hereditary syphilis as Rotch and Weiss have pointed out.

Engel found in 15 cases a low percentage of polymorphonuclear forms, 16 per cent. to 11 per cent., while the lymphocytes were considerably increased, and as many as 14 per cent. of eosinophiles occurred in some cases. Nucleated red corpuscles were found in some cases. Loos found myelocytes in 4 cases. Gundobin found the lymphocytes absolutely and relatively increased. This predominence of lymphocytes over the polymorphonuclears may disappear when malnutrition or complications in the gastrointestinal tract and lung occur.

DISEASES OF THE RESPIRATORY TRACT.—Slight acute inflammatory processes of the respiratory tract may cause oligochromemia and oligocythemia; chronic processes scarcely ever do. The leucocytes generally increase in number according to the severity of the process; slight leukocytosis occurring in the acute catarrhal processes and enormous increase in number when more tissue is involved and the severity of the process is pronounced.

In conditions producing cyanosis there may be increase in the number of red and white corpuscles and in the percentage of hemoglobin. Grawitz found such to be the case in asthma and heart diseases. The polymorphonuclear cells usually contribute the leucocytic increase; the eosinophiles are either not affected or absent altogether in the majority of processes, excepting in asthma of the bronchial type when they are generally spoken of as prominent. Schreiber in his lectures claims that they are not peculiar to this type but are found in all types in the blood and secretions.

In bronchitis there may be slight leukocytosis with especial increase of the lymphocytes or mononuclear cells. The average count and differential count of cases reported by Gundobin is: total 17,500; lymphocytes 42 per cent., mononuclear 8 per cent., polymorphonuclear 50 per cent., and eosinophiles 2 per cent. Weiss found in cases not specially classified as acute or chronic moderate leukocytosis with particular increase of the mononuclear forms. In one of the cases in which nasal complications existed he found an increase of the eosinophiles.

GASTROINTESTINAL DISEASES.—The condition of the blood varies according to the extent of the process, the duration, and the existence or non-existence of diarrhea and vomiting. Profuse diarrhea or vomiting may for a time thicken the blood by loss of water. Hoch and Schlessinger found that such inspissation with consequent increase of specific gravity does not occur until the drain has existed for some time and the tissues as well as the blood have been affected. There is no change in the blood, according to their investigations, when the amount of water lost is equalled by the quantity ingested. When the ingestion is less than the excretion the tissues first contribute and the blood secondarily.

The differential count of the leucocytes, according to Weiss, shows an especial increase of the lymphocytes and transitional leucocytes.

RACHITIS.—In rickets there is no typical blood-picture. The changes found vary with the severity of the affection, its duration, and the involvement of the inner organs. In the moderate grades there is usually a reduction of red corpuscles and a decrease of the hemoglobin with an accompanying leukocytosis. In severe cases these conditions become pronounced. Weiss found increase of the mononuclear forms and transitional leucocytes. The neutrophiles were decreased. Loos found nucleated reds, myelocytes, polychromatophilia. The red corpuscles in some cases show enormous reductions in a comparatively short space of time (v. Jaksch, Luzet.)

CUTANEOUS DISEASES.—Increase in the number of eosinophiles has been observed in a variety of skin diseases, but the cause of the increase is entirely unknown.

NERVOUS DISEASE.—In the functional disorders of childhood there may be a moderate grade of anemia, though this is often less marked than the appearance of the skin would indicate. Burr has found that the blood in chorea is not as a rule anemic.

METHOD OF EXAMINATION.

In our own examinations of the blood in childhood, we have enumerated the corpuscles and estimated the hemoglobin in all cases and have made differential counts of the leucocytes. In some cases we have estimated the specific gravity of the blood, but have not pursued this as a routine. In the histological examination of the blood, various methods of preparation were used; the films were fixed with heat, mixtures of absolute alcohol and ether, solutions of bichlorid of mercury, picric acid, etc. These various methods were employed because we were particularly desirous of discovering any signs of nuclear change which might escape detection by the ordinary method of fixation with heat. The stains used were eosin and hematoxylon, Canon's stain, and Ehrlich's triple stain.

Our examinations have shown practically no differences in the morphology of the red corpuscles in childhood as compared with the adult. Polychromatophilia and irregularities of shape and size of the red cells were perhaps more conspicuous in the moderate anemias than in the adult and nucleated red corpuscles were found in some cases in which the degree of anemia would not have led us to expect their occurrence in adults. In no case was granular basic degeneration observed.

In the study of the white corpuscles certain peculiarities were observed that merit especial mention. There was a decidedly greater tendency to basic staining than we had been accustomed to observe in adult blood. The lymphocytes stained with Canon's mixture in many cases presented a coarse granular protoplasm while the nucleus stained a light blue. Occasionally this granular character assumed the appearance of distinct granulations and in some instances these granulations were extruded from the cell, projecting as little knob-like masses. These of course suggested artefacts, but if so the occurrence of the coarse granular bodies in the protoplasm indicated that there was before the extension a differentiated condition of the protoplasm and that the extruded particles represented performed elements and not artefacts pure and simple. In the large mononuclear cells we found in a number of instances minute basic or amphophilic granules. Even when amphophilic these rather inclined to basic than acid affinity. These granules were closely set and gave the protoplasm of the cell a fine dusted appearance. Coarse basophilic granules were occasionally found in these cells, but never distinct mast-cell granules. The polymorphonuclear cells in a few instances contained very sharply defined and quite abundant basophilic granules. These were larger than the neutrophile granules usually observed, but were smaller than mast-cell granules. They stained with great intensity and therefore gave the cell a very striking appearance. Mast-cells were found in some cases but were not abundant in any instance. Upon the whole, the basophilic granules were much more conspicuous in the blood of childhood than they have usually been found or we have found them in the blood of adults.

Myelocytes were observed in a number of cases (10 out of a total 49) as will be seen in the special notes. We could find no particular significance in their occurrence. In connection with what has been said before regarding the prognostic significance of myelocytes, it may be noted that one of the most severe cases of pneumonia ending fatally showed as many as 2.2 per cent. of myelocytes at one of the examinations.

The blood counts in general have shown no striking peculiarities. The number of leucocytes was usually high as compared with the numbers found in adults excepting in the case of typhoid fever in which the leucopenia usually observed was found. Transitional leucocytes were estimated with the large mononuclears.

We may now refer to the cases in detail and summarize the observations after the histories of the cases.

PNEUMONIA.

CASE I.—Helen D., aged nine years, was admitted to the hospital with croupous pneumonia. There is nothing of interest in the clinical history which was incomplete.

The blood count showed: 4,460,000 red blood corpuscles; 29,200 white blood corpuscles; 85 per cent. of hemoglobin. The differential count showed: 87 per cent. polymorphonuclears, 9.4 per cent. mononuclears, 3.6 per cent. lymphocytes, 0.4 per cent. myelocytes.

The following notes were made regarding the appearance of the stained specimens: Canon stain—protoplasm of the leucocytes not well stained but nuclei dark; mononuclears and lymphocytes sometimes difficult to differentiate. Specimens fixed with heat showed some polychromatophilia. Triple stain—distinct myelocytes were discovered.

CASE II.—Lazer T., aged two years and three months. The patient was admitted with pneumonia of the right side, and there were râles throughout the other lung as well. The child was rachitic and the temperature was constantly high. The spleen and liver were both easily palpable, and the former considerably enlarged. Purpuric spots developed on the abdomen. The abdomen subsequently became swollen by tympany. After an illness of some weeks, the child died. No autopsy.

The blood count soon after admission showed: 4,332,000 red blood corpuscles; 68,000 white blood corpuscles; and 56 per cent. of hemoglobin. The differential count showed: 59.6 per cent. polymorphonuclears, 6.4 per cent. mononuclears, 30.4 per cent. lymphocytes, 1.4 per cent. eosinophiles, 2.2 per cent. myelocytes. The second examination, some days later, showed 87,200 white blood corpuscles and 55 per cent. of hemoglobin.

The differential count was then 49.6 per cent. of polymorphonuclears, 8.8 per cent. mononuclears; 39.6 per cent. lymphocytes, 1.4 per cent. eosinophiles (polymorphonuclear), 0.1 per cent. mononuclear eosinophiles, 0.5 per cent. myelocytes. The last examination made towards the end of the illness showed: 3,440,000 red blood corpuscles, 27,824 white blood corpuscles; 46 per cent. of hemoglobin. The differential count showed 47.5 per cent. polymorphonuclears, 13.9 per cent. mononuclears, 37.4 per cent. lymphocytes, 0.8 per cent. eosinophiles, 0.4 per cent. myelocytes.

Examination of the stained specimens showed as follows: triple stain—red blood corpuscles irregular in shape; some large flabby forms; some polychromatophilia; large and small nucleated reds with clover leaf multipartite nuclei. No karyokinesis. Picric acid specimens stained with eosin and hematoxylon showed about the same conditions, and one nucleated corpuscle with a karyokinetic figure. Canon stain (fixed by alcohol and ether)—same conditions of red corpuscles and leucocytes; some of the polymorphonuclear forms contain sparse basophilic granules which stand out very distinctly; some of the lymphocytes show the same granules, the latter were decidedly more coarse than the δ-granules of Ehrlich. Practically, the same conditions were found in the specimens fixed by heat, and in those fixed with bichlorid of mercury.

CASE III.—Sarah M., aged four years, had had measles which was followed by a loose cough and dulness of the left lung. The first examination of the blood showed: 4,540,000 red blood corpuscles; 35,200 white blood corpuscles; 85 per cent. of hemoglobin. The differential count showed 71.6 per cent. polymorphonuclears; 10.5 per cent. mononuclears; 17.9 per cent. lymphocytes. The second examination, ten days later, when the child was convalescing, showed: 4,312,500 red blood corpuscles; 18,600 white blood corpuscles; and 90 per cent. of hemoglobin. The differential count showed: 70.5 per cent. of polymorphonuclears, 13.3 per cent. mononuclears, 16.2 per cent. lymphocytes, and 0.2 per cent. myelocytes.

The examination of the stained specimens at the first examination showed slight polychromatophilia, but nothing else of consequence. At the second examination, some poikilocytosis and a few shadow corpuscles were discovered.

CASE IV.—William M., aged four and a half years, was admitted to the hospital with double lobar pneumonia, and developed pericarditis and acute general peritonitis. The examination of the blood soon after admission showed 5,025,000 red blood corpuscles; 34,688 white blood corpuscles; 78 per cent. hemoglobin. The differential count showed 86.1 per cent. polymorphonuclears, 6.2 per cent. mononuclears, 7.6 per cent. lymphocytes, and 0.1 myelocytes.

The microscopic examination showed as follows: Canon stain (fixed by heat)—red corpuscles irregular, some shadow forms, and some polychromatophilia; no nucleated forms; occasional distinct coarse granules in mononuclears and lymphocytes; transition between the polymorphonuclear and the ordinary transitional leucocytes less sharply defined than in normal blood; myelocytes very large. Specimens fixed with picric acid, bichlorid and alcohol and ether showed nothing additional. In the specimens stained with the triple stain, typical myelocytes were found.

CASE V.—Annie S., aged eighteen months. Tuberculous history in mother. Child's illness began with a convulsion, followed by repeated convulsions. No retraction of head. Croupous pneumonia developed. Doubtful meningitis. No autopsy. The blood count showed: 4,962,500 red blood corpuscles; 32,160 white blood corpuscles; and 70 per cent. of hemoglobin. The differential count showed: 84.3 per cent. polymorphonuclears, 8.1 per cent. mononuclears, 7.6 per cent. lymphocytes.

The microscopical examination showed: Canon stain—red corpuscles normal in appearance, though the central parts stain unusually little; mononuclear leucocytes were of two kinds—(1) some with large pale nucleus and slightly granular protoplasm, (2) others of smaller size with dense granulation. A few excessively large, but otherwise typical mononuclear cells were seen; the lymphocytes frequently had a granular zone about the nucleus. Specimens stained with other methods showed nothing additional.

CASE VI.—Josephine G., aged about six years, was admitted with pneumonia of the right lung and had an axillary abscess on the left side. The blood count showed: 3,386,000 red blood corpuscles; 20,400 white blood corpuscles; 69 per cent. of hemoglobin. The differential count showed: 52.6 per cent. polymorphonuclears, 15.9 per cent. mononuclears, 31.5 per cent. lymphocytes, and there were one thousand nucleated red corpuscles per cubic millimeter.

The microscopical examination showed: Canon stain—slight poikilocytosis; distinct nucleated red corpuscles with clover leaf and multipartite nuclei. Many of the nucleated cells showed polychromatophilia. Mononuclear leucocytes often had distinctly basophilic granular protoplasm. Nothing additional was discovered by other methods.

CASE VII.—Jacob H., aged five and a half years, had had pneumonia at two years of age and was weakly. His present attack began a week before admission. The child was rachitic, and there was a mucopurulent discharge from the nose. Croupous pneumonia of the right apex was discovered. The blood count showed: 3,506,200 red blood corpuscles; 50,917 white blood corpuscles; and 83 per cent. hemoglobin. The differential count was 73 per cent. polymorphonuclears, 11.3 per cent. mononuclears, 14.7 per cent. lymphocytes, 0.9 per cent. eosinophiles and 0.1 myelocytes.

The stained specimens showed: Canon stain—red corpuscles somewhat irregular in shape, but not definitely altered; mononuclear leucocytes slightly granular; some quite large forms with indefinite pale nucleus, probably myelocytes; granular ring surrounded nucleus of lymphocytes; eosinophiles contain very small granules. Nothing additional in the other methods of staining.

In the seven cases myelocytes were found in five though usually in small numbers. In Case II. the percentage reached 2.2 per cent., but this case occurred in a rachitic child and there was besides a hemorrhagic tendency that may have been due to other causes than the pneumonia. Nucleated red corpuscles were found in two of the cases aged respectively two and a quarter and six years. In the former the anemia was marked but in the latter in which the number of erythroblasts was very considerable the anemia was not pronounced. The discovery of a nucleated red corpuscle showing karyokinesis in the one case was noteworthy, though no special significance can be given to this fact. In these cases eosinophile cells were found during the course of the disease when they were discovered at all, but in five of the cases none were found at any stage.

TYPHOID FEVER.

CASE I.—Selina N. P., aged eight years, was admitted with typhoid fever. In addition there was intense bronchitis, with occasional blood-tinged expectoration. This may have been due to bleeding in the mouth. The history is incomplete and the diagnosis somewhat in doubt. Examination of the blood showed: 4,122,500 red blood corpuscles; 27,636 white blood corpuscles; and 77 per cent. of hemoglobin. The differential count showed: 78 per cent. polymorphonuclears, 13.5 per cent. mononuclears, 8.5 per cent. lymphocytes.

The microscopic examination: Canon stain—red and white corpuscles normal in appearance. Some of the lymphocytes present dark basophilic granulation of protoplasm. A few of the red corpuscles are of unusual size.

CASE II.—Theresa K., aged twelve years. The blood count showed: 5,025,000 red blood corpuscles; 6,966 white blood corpuscles, and 77 per cent. of hemoglobin, before a tub bath. The leucocytes counted after a tub bath numbered 13,066. The differential count of the specimen, before the bath, showed: 85.7 per cent. polymorphonuclears; 8.1 per cent. mononuclears: 6 per cent. lymphocytes and 0.2 per cent. myelocytes. After the tub bath there was an increase of the polymorphonuclear leucocytes.

The microscopic examination showed great irregularity in the quality and in the size of the polymorphonuclear cells, as well as in the number and distinctness of the granules. A few definite myelocytes, and several cells of doubtful classification, but probably myelocytes were found. The red corpuscles were rather irregular in shape.

CASE III.—Rachel H., aged twelve years, was admitted in a relapse of typhoid fever which proved of short duration. The blood count showed: 3,320,000 red blood corpuscles; 6,948 white blood corpuscles; and 78 per cent. hemoglobin. The differential count: 55.3 per cent. polymorphonuclears; 9.4 per cent. mononuclears; 34.3 per cent. lymphocytes; 0.9 per cent. eosinophiles.

The microscopic examination showed great irregularity in the size and depth of color of the red corpuscles. Numerous poikilocytes were found, but no nucleated forms or polychromatophilia.

CASE IV.—Ambrose L., aged eleven years, was admitted in the early stages of typhoid fever. Four days after admission, there was some pain in the region of the heart and a rough sound suggesting pericarditis, was discovered. It disappeared, however, in two or three days without effusion. The blood count upon admission showed: 4,565,000 red blood corpuscles; 4,207 white blood corpuscles; and 70 per cent. hemoglobin. The differential count was: 75.4 per cent. polymorphonuclears; 11.6 per cent. mononuclears; 12.4 per cent. lymphocytes; 0.6 per cent. myelocytes. Two hours later after a tub bath there were found: 3,800 white blood corpuscles, and the differential count was 78.7 per cent. polymorphonuclears; 9.5 per cent. mononuclears; 10.2 per cent. lymphocytes; 0.8 per cent. eosinophiles; 0.8 per cent. myelocytes. The examination of the blood during convalescence showed: 4,830,000 red blood corpuscles; 12,320 white blood corpuscles; 80 per cent. hemoglobin. The differential count: 66.5 per cent. polymorphonuclears; 11.7 per cent. mononuclears; 21.6 per cent. lymphocytes; 0.2 per cent. eosinophiles.

The microscopic examination: the red corpuscles were somewhat distorted, and showed a tendency to polychromatophilia, though this was not marked. The lymphocytes were very small and with excessively dark nuclei. A few myelocytes were found and one of these was of excessive size.

CASE V.—Bessie J., was admitted rather late in the course of typhoid fever. The blood count showed: 3,716,000 red blood corpuscles; 6,880 white blood corpuscles; and 70 per cent. of hemoglobin. The differential count showed: 36.3 per cent. polymorphonuclears; 27.3 per cent. mononuclears; 35.8 per cent. lymphocytes; 0.6 per cent. eosinophiles. A short relapse occurred, and the blood count during this (and after a tub bath) showed: 3,850,000 red blood corpuscles; 9,840 white blood corpuscles; and 70 per cent. hemoglobin.

The microscopic examination of the stained specimens showed: Canon stain—a tendency to basophilic protoplasm in the mononuclear cells. There were two mononuclear cells with distinct basophilic granules.

CASE VI.—Thomas McK., aged ten years, had been in bad health for several months, with some cough. When admitted he was evidently in the first week of typhoid fever. There was rather more bronchitis than usual, and the mucopurulent expectoration was occasionally blood stained. The blood count showed: 5,120,000 red blood corpuscles; 9,266 white blood corpuscles; and 75 per cent. of hemoglobin. The differential count: 69.4 per cent. polymorphonuclears; 10.6 per cent. mononuclears; 20 per cent. lymphocytes.

The microscopic examination: Canon stain—red corpuscles uniformly somewhat purplish in color. The leucocytes were large and small and the former were rather difficult to distinguish from the mononuclear cells. In the latter, the nucleus was deeply stained and the protoplasm light colored. In one case, however, a very large mononuclear contained a pale nucleus and deeply stained protoplasm. In the specimens fixed with bichlorid, one polymorphonuclear cell was found with distinct basophilic granules. A few cells were found which are recorded as "doubtful myelocytes."

CASE VII.—Laura G. had typhoid fever and developed a bronchopneumonia. The blood count was made late in the case when the convalescence was practically established. There were 5,200,000 red blood corpuscles; 20,928 white blood corpuscles; and 76 per cent. of hemoglobin. The differential count showed: 17.3 per cent. polymorphonuclears; 50.7 per cent. mononuclears; 32 per cent. lymphocytes.

The microscopic examination showed marked irregularity in shape and some excessively large red blood corpuscles; a few shadow cells and all of the red corpuscles poorly stained.

CASE VIII.—Harry B., aged about six years, was admitted in the second week of typhoid fever. There was slight bronchitis. The blood count was as follows: 4,200,000 red blood corpuscles; 7,000 white blood corpuscles; 78 per cent. hemoglobin. The differential count: 53.1 per cent. polymorphonuclears; 16.7 per cent. mononuclears; 30.2 per cent. lymphocytes. A second count was made during the convalescence from the typhoid fever and the following figures were obtained: 4,360,000 red blood corpuscles; 8,342 white blood corpuscles; 68 per cent. hemoglobin. The differential count: 52.9 polymorphonuclears; 16.4 per cent. mononuclears; 30.7 per cent. lymphocytes.

The microscopic examination of the stained specimens showed: red corpuscles large, irregular in shape and in size, and one distinct nucleated corpuscle of a rather large size with central deeply staining nucleus, surrounded by a clear space. Among the leucocytes were several large forms with excentric nuclei having irregular outlines; they resembled myelocytes. A number of fragmented leucocytes were seen. In the specimen stained with Canon stain some polychromatophilia was seen. The microscopic examination of the specimen during convalescence showed nothing abnormal.

CASE IX.—Benjamin S., aged eight years, was admitted with well developed typhoid fever, and had a few râles indicative of bronchitis. There was paroxysmal cough which developed into distinct pertussis and an eruption of varicella occurred a week after admission. Examination of the blood at the time of admission showed: 3,808,000 red blood corpuscles; 20,800 white blood corpuscles; and 83 per cent. hemoglobin. The differential count: 81.6 per cent. polymorphonuclears, 6.2 per cent. mononuclears, 10.4 per cent. lymphocytes, and 1.8 per cent. eosinophiles.

The microscopic examination showed: red corpuscles normal in appearance for the most part but one distinct megaloblast, a number of microblasts, and some shadow corpuscles and fragmented cells were found.

In these cases the absence of leukocytosis, noted in adults, was found in all excepting three; and in these complications (severe bronchitis, pneumonia, and pertussis and varicella) were sufficient to explain the increased number of leucocytes. The differential counts of leucocytes were not characteristic but the occurrence of myelocytes in at least three of the cases is notable.

PERTUSSIS.

CASE I.—Marie G., aged twenty-two months, a rachitic child, was admitted with a cough, which had existed for six weeks. Sibilant râles were discovered in both lungs and characteristic whoops developed in a few days. The blood count showed 5,700,000 red blood corpuscles; 12,145 white blood corpuscles; 82 per cent. hemoglobin. The differential count: 40.8 per cent. polymorphonuclears; 27.8 per cent. mononuclears; 24 per cent. lymphocytes; 5.6 per cent. eosinophiles; 1.8 per cent. myelocytes.

Microscopic examination showed: the red corpuscles were equal in size and well-stained. There was much variability in the appearance of the individual types of leucocytes; some of the mononuclear being very similar in appearance to lymphocytes; others more typical according to the ordinary description. Similarly, the lymphocytes varied from small bodies in which the nucleus and protoplasm were scarcely distinguishable to large forms approaching the large mononuclear. Both neutrophilic and eosinophilic myelocytes were observed.

CASE II.—X. Y., aged about four years, was admitted with whooping-cough. The blood count showed: 4,545,000 red blood corpuscles; 34,667 white blood corpuscles; 88 per cent. hemoglobin. The differential count: 29.2 per cent. polymorphonuclears; 17.4 per cent. mononuclears; 52.6 per cent. lymphocytes; 0.8 per cent. eosinophiles; 0.1 per cent. myelocytes.

Nothing of consequence beyond the existence of myelocytes in the microscopical examination.

CASE III.—Theodore W., aged six was first admitted to the hospital with malaria, but subsequently developed pertussis. At that time the blood count showed: 4,187,500 red blood corpuscles; 16,218 white blood corpuscles; 73 per cent. hemoglobin. The differential count: 41.4 per cent. polymorphonuclears; 19.5 per cent. mononuclears; 36.9 per cent. lymphocytes; 2.2 per cent. eosinophiles. The microscopic examination: normal red cells; a number of degenerated mononuclear cells; otherwise no abnormality.

In three cases the most striking peculiarity was the marked increase of lymphocytes. This may be of interest in connection with the supposed disease of the lymph glands in this disease.

VARICELLA.

CASE I.—William G., aged seven and a half years, developed varicella in the house. The child was of rather strumous appearance. During the attack, the blood count showed: 4,743,700 red blood corpuscles; 7,466 white blood corpuscles, and 75 per cent. hemoglobin. The differential count: 56.5 per cent. polymorphonuclears; 19.1 per cent. mononuclears; 23.4 per cent. lymphocytes; 1 per cent. eosinophiles.

The microscopic examination showed some inequality of red corpuscles with occasional macrocytes and slight polychromatophilia.

CASE II.—Harry B., aged two years and eight months, was first admitted to the hospital with typhoid fever from which convalescence was rapid. He developed varicella two weeks and five days after admission, and had a copious eruption. During the attack, the blood count showed: 7,440 leucocytes. The count of red corpuscles and the amount of hemoglobin were not preserved. The differential count showed: 46 per cent. polymorphonuclears; 16.4 per cent. mononuclears; 36.4 per cent. lymphocytes; 1 per cent. eosinophiles; and 0.2 per cent. myelocytes. There was nothing of any consequence in the microscopical examination.

CASE III.—William M., aged six months, ill developed child, with some cough, and bronchial râles, developed varicella in the hospital, and afterwards had pneumonia and died. During the period of varicella, the blood count showed: 5,300,000 red blood corpuscles; 19,360 white blood corpuscles; and 98 per cent. hemoglobin. The differential count showed: 70.2 per cent. polymorphonuclears; 16.6 per cent. mononuclears; 12.8 per cent. lymphocytes; 0.4 per cent. eosinophiles.

The microscopic examination showed well stained and normal red corpuscles; one nucleated red corpuscle was found. The mononuclear leucocytes were frequently degenerated or fragmented in appearance; some were distinctly so and had jagged outline. There was occasional hyperchromatosis.

CASE IV.—William S., aged four years, developed varicella in the hospital. The blood count showed: 5,330,000 red blood corpuscles; 12,800 white blood corpuscles; and 90 per cent. hemoglobin. The differential count showed: 44.9 per cent. polymorphonuclears; 20.5 per cent. mononuclears; 33.8 per cent. lymphocytes; 0.8 per cent. eosinophiles.

The microscopic examination: red blood corpuscles stained poorly, and were somewhat irregular in shape. The mononuclear cells were very variable in size and many were excessively large. Some of these large forms contained granular basophilic protoplasm; others were entirely clear. The same characters of protoplasm were observed in the lymphocytes, and attached to the latter were occasionally granular particles entirely outside of the cells but attached by small threads.

TUBERCULOUS CARIES WITH COLD ABSCESS.

Edward F., aged about ten years, was admitted to the surgical ward with a mass in the abdomen which was regarded as a solid growth, but which subsequently showed itself to be fluctuating, and eventually was found to be a tuberculous collection secondary to necrosis of the lumbar vertebræ.

The blood count showed: red blood corpuscles 4,500,000; white blood corpuscles 20,579; hemoglobin 66 per cent. The differential count showed: polymorphonuclear cells 70.3 per cent.; mononuclear 18.1 per cent.; lymphocytes 10.7 per cent.; eosinophiles 0.9 per cent.

The microscopic examination of the stained specimens showed some distortion of the red corpuscles. Several polymorphonuclear cells with distinct basophilic granules were discovered. These were quite distinctly different from the basophilic granules of the mononuclear cells, which were fine and indistinctly stained. The ones in the polymorphonuclear on the contrary were coarse and occasionally larger than the granules of the eosinophiles. The mononuclear cells generally showed a basophilic protoplasm with occasionally fine but indistinct granulation. The differentiation of the mononuclear cells and lymphocytes was very difficult, and the differential count is possibly erroneous in giving too great a proportion of mononuclear cells. There was no polychromatophilia.

ACUTE RHEUMATISM.

Jacob F., aged five years, was admitted with pain in the back and legs. The legs were exceedingly tender to the touch. The ankles were slightly swollen and tender; there was constipation. The history indicated a subsiding articular rheumatism.

The blood count showed: 4,355,000 red blood corpuscles; 7,022 white blood corpuscles, and 75 per cent. hemoglobin. The differential count showed: polymorphonuclears 59 per cent., mononuclears 22.4 per cent., lymphocytes 17.6 per cent., eosinophiles 1 per cent.

On microscopic examination of the stained specimens the red corpuscles were found deeply colored but entirely normal in appearance. Among the polymorphonuclear leucocytes, several were found with deeply staining protoplasm (somewhat acidophilic) and with vacuoles. Vacuolated mononuclear cells were also seen. One of the latter forms contained numerous vacuoles and another mononuclear cell contained very distinct and rather coarse basophilic granules scattered throughout the cell and over the nucleus.

NOMA.

CASE I.—Helen O'D., aged about seven years, was admitted with a history of vague illness beginning about two weeks before entrance into hospital. There had been slight cough and abdominal pain. The temperature on admission was 103.2° F. The spleen was slightly enlarged, and there were a few suspicious spots on the abdomen. Tongue coated but not characteristic; lungs clear. The appearance was like that of a typhoid case, but the history was uncertain and Widal test negative. Delirium occurred and the face became swollen. A bad tooth was discovered and noma developed. Curetted and cauterized. Rapid progress, extreme gangrene and death after eleven days.

The blood counts showed:

1st count on admission: Red blood corpuscles, 5,380,000; leucocytes, 9,822; hemoglobin, 80 per cent.

2d count three days later: Red blood corpuscles, 4,185,000; leucocytes, 5,058; hemoglobin, 65 per cent.

3d count day before death: Red blood corpuscles, 3,260,000; leucocytes, 12,144; hemoglobin, 58 per cent.

The differential counts were as follows:

1st count: Polymorphonuclears, 86.4 per cent.; mononuclears, 7.4 per cent.; lymphocytes, 5.8 per cent.; eosinophiles, 0.4 per cent.

2d count: Polymorphonuclears, 72.5 per cent.; mononuclears, 13 per cent.; lymphocytes, 14.5 per cent.

3d count: Polymorphonuclears, 74.5 per cent.; mononuclears, 16.3 per cent.; lymphocytes, 9.2 per cent.

The microscopic examination at the time of the first count showed some poikilocytosis and dark chromatin masses in the polymorphonuclear leucocytes. At the second count nothing of note was observed excepting a fine chromatin net work in the protoplasm of many polymorphonuclear cells, suggesting basophilic granules; and a similar condition in lymphocytes as well as projecting strands with distinctly bulbous extremities; occasional hyperchromatosis was found in the mononuclears. The neutrophilic granules varied in coarseness in different polymorphonuclear cells.

Third examination: Irregularity of the red corpuscles in size and shape; uneven staining. Occasional pseudovacuolation and slight polychromatophilia; megalocytes. All forms of the leucocytes when stained with Canon's stain showed here and there basophilic granules, which in some of the mononuclears seemed quite clearly to be nodal points in a protoplasmic network. The polymorphonuclear cells frequently contained basophilic granules and some had very pronounced granulations of this sort.

BRONCHITIS.

CASE I.—Louise B., aged four years, was admitted to the hospital with fever and the evidences of pulmonary disease. There were scattered moist râles on both sides and a suspicion of dulness at the right base, but no positive dulness. The diagnosis of catarrhal pneumonia was made. Examination of the blood showed 5,126,000 red blood corpuscles; 14,619 white blood corpuscles; 92 per cent. hemoglobin.

CASE II.—Jennie H., aged five years, had suffered with purulent otitis since her first year. Her mother had died of phthisis, and there had been five or six miscarriages. Five or six children died young. The diagnosis of bronchitis and subacute pneumonia was made. The blood examination showed 3,875,000 red blood corpuscles; 15,300 white blood corpuscles, and 65 per cent. hemoglobin. The differential count: 63.4 per cent. polymorphonuclears; 12.5 per cent. mononuclears; 22.9 per cent. lymphocytes, and 1.2 per cent. eosinophiles.

The microscopical study of the specimens: Canon's stain—red corpuscles normal; mononuclear leucocytes very large with poorly stained nucleus, and occasionally deep granular protoplasm; lymphocytes both large and small; protoplasm stained deeply with methylene blue. Nothing of interest observed in the specimens fixed and stained by other methods.

CASE III.—Mary McC., aged four years, was admitted with acute bronchitis and slight diarrhea. There were râles on both sides of the chest; also some slight acute tonsillitis and pharyngitis, with enlargement of the lymphatic glands of the neck. The blood count showed 5,390,000 red blood corpuscles; 19,226 white blood corpuscles, and 96 per cent. hemoglobin. The differential count: 74.7 per cent. polymorphonuclears; 11.2 per cent. mononuclears; 12.9 per cent. lymphocytes; 1.2 per cent. eosinophiles.

The stained specimens: Canon's stain—red corpuscles about normal; white corpuscles showed nothing striking, excepting the pallor of the nuclei of the mononuclear forms and a tendency to granular basophilic protoplasm in the same cells. Nothing of consequence in the specimens prepared by other methods.

CASE IV.—Louis S., aged three years, was admitted with acute bronchitis. The blood count showed 5,010,000 red blood corpuscles; 12,909 white blood corpuscles; 63 per cent. hemoglobin. The differential count: 69.4 per cent. polymorphonuclears; 12.6 per cent. mononuclears; 18 per cent. lymphocytes.

The examination of the stained specimens: Canon stain—red corpuscles normal in appearance; mononuclear leucocytes frequently presented an unusually pale nucleus and granular protoplasm.

CASE V.—Theodore W., aged six years, was admitted with acute bronchitis. The blood count showed 4.958,000 red blood corpuscles; 12,691 white blood corpuscles; 83 per cent. hemoglobin. The differential count: 61.3 per cent. polymorphonuclears; 6.9 per cent. mononuclears; 29.9 per cent. lymphocytes; 1.9 per cent. eosinophiles.

The examination of the stained specimens: Canon stain—red corpuscles normal; lymphocytes occasionally had basophilic granules, but more often the protoplasm was profusely basophilic.

CASE VI.—Veronica D., aged three years, was admitted with subacute bronchitis. She had had pneumonia, but the impairment of the lung and the active signs of pneumonia had entirely disappeared. There was enlargement of both tonsils. The blood count showed 3,775,000 red blood corpuscles; 14,507 white blood corpuscles; 82 per cent. hemoglobin. The differential count: 87 per cent. polymorphonuclears; 9.4 per cent. mononuclears; 3.6 per cent. lymphocytes.

The microscopical examination: the red corpuscles were normal; white corpuscles—there were two distinct varieties of lymphocytes, large and the small; the protoplasm of the former being without granules, that of the latter stained a bluish color. The larger forms were difficult to distinguish from mononuclear cells.

Case VII.—Bessie B., aged seven and one-half years was admitted to the hospital with acute bronchitis and had moderate continuous fever. The child also had seat worms. The blood count showed 3,880,000 red blood corpuscles; 12,835 leucocytes and 78 per cent. of hemoglobin. The differential count showed: 52.3 per cent. polymorphonuclears; 15.1 per cent. mononuclears; 25.3 lymphocytes; 7.3 per cent. eosinophiles. The microscopic examination showed: some irregularity in the staining, and size and shape of the red corpuscles, with occasional polychromatophilia. The white corpuscles showed no peculiarities.

The moderate leukocytosis is the only notable condition discovered. In two or three of the cases it is likely that there were patches of bronchopneumonia, though none could be classed as an instance of pneumonia in a strict sense.

PLEURAL EFFUSION.

Case I.—Harry B., aged twenty-three months, was admitted with pleural effusion. There was marked dyspnea and slight cyanosis, and the right pleural cavity was filled to the second rib. The legs were moderately edematous; the hands less so. The blood count showed: 3,755,000 red blood corpuscles; 13,610 white blood corpuscles; 70 per cent. hemoglobin. The differential count: 37.2 per cent. polymorphonuclears; 34.5 per cent. mononuclears; 27.1 per cent. lymphocytes; 1.2 per cent. eosinophiles.

Microscopically, the red corpuscles were found unequal in size. Some distinct megaloblasts and microcytes were observed; a few polychromatophilic corpuscles were seen. The leucocytes showed no abnormalities.

ENTERITIS.

CASE I.—Eva P., aged ten months, was admitted with marked enteritis. The stools were filled with mucus, and were occasionally blood-streaked. There was a slight cough, and also a slight vaginitis. The blood count showed: 4,060,000 red blood corpuscles; 27,666 white blood corpuscles; and 65 per cent. hemoglobin. The differential count showed: 29 per cent. polymorphonuclears; 38.3 per cent. mononuclears; 31.8 per cent. lymphocytes; 0.9 per cent. eosinophiles.

The microscopical examination: Canon stain—red blood corpuscles slightly irregular in size; some polychromatophilia. Lymphocytes contained very dark nuclei; their protoplasm was usually granular and generally basophilic. Sometimes the nuclei presented themselves in ring forms.

CASE II.—Jennie M., aged six years was an ill developed child with a bad family history. The child was very anemic, and there were enlarged glands in the axilla, groins and cervical region. The appearance was that of profound inanition. The blood count showed: 5,050,000 red blood corpuscles; 16,081 white blood corpuscles and 68 per cent. hemoglobin. The differential count was 76 per cent. polymorphonuclears; 10.8 per cent. mononuclears; 13.2 per cent. lymphocytes.

The microscopic examination: red corpuscles normal; white blood corpuscles, some of the large mononuclear presented a curious vacuolated appearance, and a distinction between nucleus and protoplasm could not be made. The appearance was that of degenerated cells. The lymphocytes also presented occasional vacuolation. The specimen stained with triple stain showed many degenerate white cells.

CASE III.—Edith W., aged three months, was admitted as a case of general malnutrition. There was a tubercular history, and the child had been fed on condensed milk. Some time after its entrance to the hospital, the child developed varicella and finally it died of inanition. At the autopsy, chronic enteritis was the lesion found. The blood count prior to the varicella showed: 4,640,000 red blood corpuscles; 26,800 white blood corpuscles; 97 per cent. hemoglobin. The differential count showed: 59.6 per cent. polymorphonuclears; 15.3 per cent. mononuclears; 24.9 lymphocytes; 0.2 eosinophiles.

The microscopic examination showed no abnormality of the red corpuscles, but the leucocytes were occasionally vacuolated.

CASE IV.—William G., aged seven and a half years, was admitted to the hospital suffering with enteritis due to oxyuris. The blood count showed: 5,125,000 red blood corpuscles; 9,499 white blood corpuscles, and 94 per cent. hemoglobin.

MITRAL HEART DISEASES.

CASE I.—Emily B., aged eleven and a half years, was admitted to the hospital with double mitral valvular disease. There were occasional attacks of cyanosis; no edema nor other signs of failing compensation. The blood count showed: red corpuscles 4,390,000; leucocytes 13,658; hemoglobin 79 per cent. The differential count showed: polymorphonuclears 68.6 per cent.; mononuclears 13 per cent.; lymphocytes 18.2 per cent.; eosinophiles 0.2 per cent.

The microscopic examination showed as follows: picric acid, eosin, hematoxylon specimen: protoplasm of mononuclears and lymphocytes stained dark blue; some vacuolation; lymphocytes large and small; red corpuscles normal. Canon stain of heat—fixed specimen: protoplasm and nucleus of mononuclears hard to distinguish; slight basic granulation of the protoplasm; lymphocytes of two sizes, the larger being the paler nucleus; protoplasm in both forms dark blue.

CASE II.—Thomas S., aged six years, had rheumatic valvular disease, double mitral. He was subject to attacks of dyspnea and anasarca. The blood count showed: red corpuscles 4,975,000; leucocytes 20,587; hemoglobin 70 per cent. The differential count: polymorphonuclears 58.4 per cent.; mononuclears 13.8 per cent.; lymphocytes 25.4 per cent.; eosinophiles 2.2 per cent.; myelocytes 0.2 per cent.

The microscopic examination showed as follows: Canon stain with heat fixation. The mononuclears were of two kinds, one with pale nucleus and granular protoplasm, the other with a dark nucleus and unstained protoplasm, a few contained distinct basophilic granulations; lymphocytes were variable in size: the larger showing a basophilic protoplasm; one distinct myelocyte was found.

RACHITIS.

CASE I.—Emma F., aged nineteen months, had marked signs of rickets. The blood count showed: red blood corpuscles 5,170,000; white blood corpuscles 11,911; 78 per cent. hemoglobin. The differential count showed: polymorphonuclears 42 per cent.; mononuclears 18.4 per cent.; lymphocytes 36.6 per cent.; eosinophiles 2.6 per cent.; myelocytes 0.4 per cent.

The microscopic examination of the stained preparations showed normal red corpuscles, but several distinct peculiarities in the leucocytes. The polymorphonuclears were variable in size, the larger forms having pale nuclei and the smaller ones nuclei of the ordinary appearance. Several contained distinct basophilic granulations which were deeply stained. The same form of granules was found in several mononuclear cells. The lymphocytes were present in two varieties, some being very small with a densely stained nucleus and little protoplasm, and others large and containing pale nuclei with basophilic protoplasm. The eosinophile cells were very large and unusually full of granules. The myelocytes were exceptionally large with oval nuclei placed to one side of the cell in fine granules.

CASE II.—William G., aged twenty months, was admitted with coryza, cough, and gastric disturbances. There was some diarrhea, and the child was greatly emaciated. It was reported that he had whooped, but no confirmation of this could be obtained. There were crackling râles in the chest. The child was decidedly rachitic.

Examination of the blood showed: red blood corpuscles 6,180,000 (?); leucocytes 29,557; 64 per cent. hemoglobin. The differential count showed: polymorphonuclears 44.7 per cent.; mononuclears 19.6 per cent.; lymphocytes 34.5 per cent.; eosinophiles 1.2 per cent.

The large proportion of lymphocytes and mononuclears in these cases was the most notable condition. Several other cases of the series examined were rachitic, but this condition was subordinate to some other disease and the cases have therefore been placed under other headings.

ECZEMA.

William L., aged two years and three months, had facial eczema which had lasted for three months. Later there were patches on the abdomen and other parts of the body.

The first blood count showed: red blood corpuscles 5,200,000; white blood corpuscles 22,000; 76 per cent. of hemoglobin. Two subsequent counts of the leucocytes showed 17,541 and 10,947. The differential counts at these three examinations showed: No. 1.—37.1 per cent. polymorphonuclears; 21 per cent. mononuclears; 35 per cent. lymphocytes; 7.9 per cent. eosinophiles. No. 2.—59 per cent. polymorphonuclears; 11.6 per cent. mononuclears; 23.7 per cent. lymphocytes; 5.7 per cent. eosinophiles. No. 3.—61.2 per cent. polymorphonuclears; 17.0 per cent. mononuclears; 14.0 per cent. lymphocytes; 7.8 per cent. eosinophiles.

The microscopic examination showed some irregularity in the red blood corpuscles with distinct microcytes. The leucocytes stained well, while the protoplasm of the polymorphonuclears was pinkish in the eosin and methylene blue stains. The protoplasm of the lymphocytes was basophilic. Occasionally dark basophilic granules were found outside the lymphocytes and attached by narrow pedicles. These had the appearance of extrusion. The protoplasm of the mononuclear cells was faintly basophilic and occasionally distinct mast-cell granulations were found. The eosinophiles were prominent and of large size.

FOCAL EPILEPSY.

Harry B., aged eight years, was admitted with a history of convulsions beginning in the leg. There was no palsy nor atrophy. His station was good and reflexes normal.

Examination of the blood showed: 4,662,500 red blood corpuscles; 11,911 white blood corpuscles; and 85 per cent. hemoglobin.

The differential count showed: polymorphonuclears 48.5 per cent.; mononuclears 20 per cent.; lymphocytes 30.3 per cent.; eosinophiles 1.2 per cent.

CONVULSIONS.

A. D., aged two months, was admitted to the hospital with a history of having had convulsions. Nothing very definite was known regarding the nature of these. There was some looseness of the bowels, but not any distinct signs of disease.

The blood count taken 20 minutes after a convulsion showed: red blood corpuscles 2,520,000; leucocytes 8,800; hemoglobin 60 per cent. The differential count showed: polymorphonuclears 42.8 per cent.; mononuclears 23.2 per cent. lymphocytes 33.6 per cent.; eosinophiles 0.4 per cent.

The microscopic examination showed irregularity, degeneration, and polychromatophilia of the red corpuscles. Several of the polymorphonuclear leucocytes contained distinct basophilic granules.

SPASTIC CEREBRAL PALSY.

Victoria D., aged about five years, has been in the hospital for some time with symptoms of spastic cerebral paralysis. There were no convulsive seizures.

The blood examination showed: 4,276,250 red blood corpuscles; 15,808 white blood corpuscles; and 85 per cent. of hemoglobin.

The differential count showed: polymorphonuclears 40.6 per cent.; mononuclears 9.9 per cent.; lymphocytes 49.1 per cent.; eosinophiles 0.4 per cent.

The microscopic examination of the stained specimen showed well stained and slightly irregular red corpuscles. White corpuscles normal in every respect.

CHRONIC MENINGITIS.

Margaret M., aged three and a half years, had doubtful symptoms of chronic meningitis with occasional convulsions. She had taken potassium iodid and presented indications of iodism.

The blood count: red corpuscles 5,412,500; leucocytes 21,333; hemoglobin 85 per cent.; specific gravity 1068.

The differential count: polymorphonuclears 66 per cent. mononuclears 10.6 per cent.; lymphocytes 23.2 per cent.; eosinophiles 0.2 per cent.

The microscopic examination showed some irregularity in the shape and size of the red cells. The protoplasm of the mononuclear cells was clear, that of the lymphocytes stained deeply with methylene blue.

SUMMARY.

Case Number.	Hemoglobin.	Erythro-cytes.	Leuco-cytes.	Polymorpho-nuclear.	Mononu-clear.	Lympho-cytes.	Eosino-philes.	Myelocytes.	Diagnosis and Remarks.
1	85 per cent.	4,460,000	29,200	87.0 per cent.	9.4 per cent.	3.6 per cent.	——	0.4 per cent.	Helen D. Croupous pneumonia.
2*a*	56 per cent.	4,332,000	68,000	59.6 per cent.	6.4 per cent.	30.4 per cent.	1.4 per cent.	2.2 per cent.	Lazer T. Croupous pneumonia and rachitis.
2*b*	55 per cent.	——	87,200	49.6 per cent.	8.8 per cent.	39.6 per cent.	1.4 per cent.	0.6 per cent.	Myelocytes, 0.5. Eosinophilic myelocytes, 0.1.
2*c*	46 per cent.	3,440,000	27,824	47.5 per cent.	13.9 per cent.	37.4 per cent.	0.8 per cent.	0.4 per cent.	
3*a*	85 per cent.	4,540,000	35,200	71.6 per cent.	10.5 per cent.	17.9 per cent.	——	——	Sarah M. Croupous pneumonia.
3*b*	90 per cent.	4,312,500	18,606	70.5 per cent.	13.3 per cent.	16.2 per cent.	——	0.2 per cent.	10 days later.
4	78 per cent.	5,025,000	34,688	86.1 per cent.	6.2 per cent.	7.6 per cent.	——	0.1 per cent.	William M. Croupous pneumonia (double).
5	70 per cent.	4,962,500	32,160	84.3 per cent.	8.1 per cent.	7.6 per cent.	——	——	Annie S. Croupous pneumonia, meningitis (?).
6	69 per cent.	3,386,000	20,400	52.6 per cent.	15.9 per cent.	31.5 per cent.	——	——	Josephine G. Croupous pneumonia and axillary abscess.
7	83 per cent.	3,506,200	50,917	73.0 per cent.	11.3 per cent.	14.7 per cent.	0 9 per cent.	0.1 per cent.	Jacob H. Croupous pneumonia.
1	77 per cent.	4,125,500	27,636	78.0 per cent.	13.5 per cent.	8.5 per cent.	——	——	Selina P. Typhoid fever.
2*a*	77 per cent.	5,025,000	6,966	85.9 per cent.	8.1 per cent.	6.0 per cent.	——	0.2 per cent.	Theresa K. Typhoid fever (before tub).
2*b*	——	——	13,066	——	——	——	——	——	Theresa K. Typhoid fever (after tub) increase in the polymorphonuclear cells.

Case Number.	Hemoglobin.	Erythrocytes.	Leucocytes.	Polymorphonuclear.	Mononuclear.	Lymphocytes.	Eosinophiles.	Myelocytes.	Diagnosis and Remarks.
3	78 per cent.	3,320,000	6,948	55.3 per cent.	9.4 per cent.	34.3 per cent.	0.9 per cent.	——	Rachel H. Typhoid fever. Second relapse.
4*a*	70 per cent.	4,565,000	4,207	75.4 per cent.	11.6 per cent.	12.4 per cent.	——	0.6 per cent.	Ambrose L. Typhoid fever, immediately before tub bath.
4*b*	——	——	3,800	78.7 per cent.	9.5 per cent.	10.2 per cent.	0.8 per cent.	0.8 per cent.	Ambrose L. Typhoid fever, two hours later.
4*c*	80 per cent.	4,830,000	12,320	66.5 per cent.	11.7 per cent.	21.6 per cent.	0.2 per cent.	——	Ambrose L. Typhoid fever, in convalescence.
5*a*	70 per cent.	3,716,000	6,880	36.3 per cent.	27.3 per cent.	35.8 per cent.	0.6 per cent.	——	Bessie J. Typhoid fever.
5*b*	70 per cent.	3,850,000	9,840	——	——	——	——	——	" " relapse and after the tub bath.
6	75 per cent.	5,120,000	9,266	69.4 per cent.	10.6 per cent.	20.0 per cent.	——	——	Thomas McK. Typhoid fever.
7	76 per cent.	5,200,000	20,928	17.3 per cent.	50.7 per cent.	32.0 per cent.	——	——	Laura G. Typhoid fever and bronchopneumonia.
8*a*	78 per cent.	4,200,000	7,000	53.1 per cent.	16 7 per cent.	30.2 per cent.	——	——	Harry B. Typhoid fever.
8*b*	68 per cent.	4,360,000	8,342	52.9 per cent.	16.4 per cent.	30.7 per cent.	——	——	" " ". during convalescence.
9	83 per cent.	3,808,000	20,800	81.6 per cent.	6.2 per cent.	10.4 per cent.	1.8 per cent.	——	Benjamin S. Typhoid fever and bronchitis.
1	82 per cent.	5,700,000	12,145	40.8 per cent.	27.8 per cent.	24.0 per cent.	5.6 per cent.	1.8 per cent.	Marie G. Pertussis and rachitis.
2	88 per cent.	4,545,000	34,666	29.2 per cent.	17.4 per cent.	52.6 per cent.	0.8 per cent.	0.1 per cent.	X. Y. Pertussis.

Case Number.	Hemoglobin.	Erythrocytes.	Leucocytes.	Polymorphonuclear.	Mononuclear.	Lymphocytes.	Eosinophiles.	Myelocytes.	Diagnosis and Remarks.
3	73 per cent.	4,187,500	16,218	41.4 per cent.	19.5 per cent.	36.9 per cent.	2.2 per cent.	——	Theodore W. Pertussis and malaria, convalescence.
1	75 per cent.	4,743,700	7,466	56.5 per cent.	19.1 per cent.	23.4 per cent.	1.0 per cent.	——	William G. Varicella.
2	——	——	7,440	46.0 per cent.	16.4 per cent.	36.4 per cent.	1.0 per cent.	0.2 per cent.	Harry B. Varicella.
3	89 per cent.	5,300,000	19,360	70.2 per cent.	16.6 per cent.	12.8 per cent.	0.4 per cent.	——	William M. Varicella, pneumonia.
4	90 per cent.	5,330,000	12,800	44.9 per cent.	20.5 per cent.	33.8 per cent.	0.8 per cent.	——	William S. Varicella.
1	66 per cent.	4,500,000	20,579	70.3 per cent.	18.1 per cent.	10.7 per cent.	0.9 per cent.	——	Edward F. Tubercular caries with cold abscess.
1	75 per cent.	4,355,000	7,022	59.0 per cent.	22.4 per cent.	17.6 per cent.	1.0 per cent.	——	Jacob F. Acute rheumatism (subsiding).
1*a*	80 per cent.	5,380,000	9,822	86.4 per cent.	7.4 per cent.	5.8 per cent.	0.4 per cent.	——	Helen O'D. Noma, on admission.
1*b*	65 per cent.	4,185,000	5,058	72.5 per cent.	13.0 per cent.	14.5 per cent.	——	——	" " three days later
1*c*	58 per cent.	3,260,000	12,144	74.5 per cent.	16.3 per cent.	9.2 per cent.	——	——	" " the day before death.

Case Number.	Hemoglobin.	Erythrocytes.	Leucocytes.	Polymorphonuclear.	Mononuclear.	Lymphocytes.	Eosinophiles.	Myelocytes.	Diagnosis and Remarks.
1	92 per cent.	5,126,000	14,619	——	——	——	——	——	Louisa B. Bronchitis, catarrhal pneumonia.
2	65 per cent.	3,875,000	15,300	63.4 per cent.	12.5 per cent.	22.9 per cent.	1.2 per cent.	——	Jennie H. Bronchitis, subacute pneumonia.
3	96 per cent.	5,390,000	19,226	74.7 per cent.	11.2 per cent.	12.9 per cent.	1.2 per cent.	——	Mary McC. Bronchitis (acute), slight tonsillitis and pharyngitis.
4	93 per cent.	5,010,000	12,909	69.4 per cent.	12.6 per cent.	18.0 per cent.	——	——	Louis S. Bronchitis (acute).
5	83 per cent.	4,958,000	12,690	61.3 per cent.	6.9 per cent.	29.9 per cent.	1.9 per cent.	——	Theodore W. Bronchitis (acute).
6	82 per cent.	3,775,000	14,507	87.0 per cent.	9.4 per cent.	3.6 per cent.	——	——	Veronica D. Bronchitis (subacute).
7	78 per cent.	3,880,000	12,835	52.3 per cent.	15.1 per cent.	25.3 per cent.	7.3 per cent.	——	Bessie B. Bronchitis (acute).
1	70 per cent.	3,755,000	13,610	37.2 per cent.	34.5 per cent.	27.1 per cent.	1.2 per cent	——	Harry B. Pleural effusion.
1	65 per cent.	4,060,000	27,666	29.0 per cent.	38.3 per cent.	31.8 per cent.	0.9 per cent.	——	Eva P. Chronic catarrh, enteritis and vaginitis.
2	68 per cent.	5,050,000	16,081	76.0 per cent.	10.8 per cent.	13.2 per cent.	——	——	Jennie M. Chronic enteritis and inanition.
3	97 per cent.	4,640,000	26,800	59.6 per cent.	15.3 per cent.	24.9 per cent.	0.2 per cent.	——	Edith W. Chronic enteritis and inanition.
4	94 per cent.	5,125,000	9,499	——	——	——	——	——	William G. Enteritis following intestinal parasites.

Case Number.	Hemoglobin.	Erythrocytes.	Leucocytes.	Polymorphonuclear.	Mononuclear.	Lymphocytes.	Eosinophiles.	Myelocytes.	Diagnosis and Remarks.
1	79 per cent.	4,390,000	13,658	68.6 per cent.	13.0 per cent.	18.2 per cent.	0.2 per cent.	———	Emily B. Mitral stenosis and regurgitation.
2	70 per cent.	4,975,000	20,587	58.4 per cent.	13.8 per cent.	25.4 per cent.	2.2 per cent.	0.2 per cent.	Thomas S. Mitral stenosis and regurgitation.
1	78 per cent.	5,170,000	11,911	42.0 per cent.	18.4 per cent.	36.6 per cent.	2.6 per cent.	0.4 per cent.	Emma F. Rachitis.
2	64 per cent.	6,180,000	29,557	44.7 per cent.	19.6 per cent.	34.5 per cent.	1.2 per cent.	———	William G. " severe diarrhea, emaciation.
1*a*	76 per cent.	5,200,000	22,000	37.1 per cent.	21.0 per cent.	35.0 per cent.	7.9 per cent.	———	William L. Eczema.
1*b*	———	———	17,541	59.0 per cent.	11.6 per cent.	23.7 per cent.	5.7 per cent.	———	" "
1*c*	———	———	10,947	61.2 per cent.	17.0 per cent.	14.0 per cent.	7.8 per cent.	———	" "
1	85 per cent.	4,662,500	11,911	48.5 per cent.	20.0 per cent.	30.3 per cent.	1.2 per cent.	———	Harry B. Focal epilepsy.
1	60 per cent.	2,520,000	8,800	42.8 per cent	23.2 per cent.	33.6 per cent.	0.4 per cent.	———	Antonio D. Convulsions.
1	85 per cent.	4,276,250	15,808	40.6 per cent.	9.9 per cent.	49.1 per cent.	0.4 per cent.	———	Victoria D. Spastic cerebral palsy.
1	85 per cent.	5,412,500	21,333	66.0 per cent.	10.6 per cent.	23.2 per cent.	0.2 per cent.	———	Margaret M. Chronic meningitis.

Extracted from The American Journal of the Medical Sciences, September, 1901.

GRANULAR DEGENERATION OF THE ERYTHROCYTE.[1]

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(*From the William Pepper Laboratory of Clinical Medicine, Phebe A. Hearst Foundation.*)

Granular, basic, or punctate degeneration of the erythrocyte is a condition in which this cell presents fine or coarse granules that have an affinity for basic stains. This degeneration affects cells which show other evidences of pathological change, as poikilocytosis and polychromatophilia, or may be present in a cell which in all other appearances is normal. Further, it may be seen in nucleated erythrocytes, where it shows absolutely no relation to the nucleus. In size the granules may be so small that they can scarcely be seen, or so large as to be nearly the size of the eosinophile granule. The shape is usually rounded, though pear-shaped, and, exceptionally, rod forms are encountered. Cells may show one or the other sized granules, or a mixture of both. The granules are usually equally distributed throughout, or small clumps may be seen in different parts of the cell. This latter arrangement is especially marked in the early stages of experimental productions and is rare in blood from the human subject. There may be a few large or fine granules scattered in the cell, or countless numbers densely packing the cell and to a great extent obscuring the intergranular substance.

It is impossible to detect this form of degeneration either in the fresh blood or in dried and unstained mounts.

Attention has been called to these granules as a special form of degeneration only in the past few years. Their presence in the circulating peripheral blood had been undoubtedly observed for a much longer period. The earlier writers, Geelmyden, Hausemann, V. Noorden, Loos, Askanazy, Shuman, Lazarus, Klein, Zenomi, and Lenoble observed such granules; and lately Litten, Krause, Bouchart, and Grawitz (in his first publications) called attention to cells with minute basic granules, which they thought were products of fragmentation (karyorrhexis) of the erythroblast, and, indeed, this view has not been wholly abandoned at the present date. Others have confounded them with polychromatophilic changes, and Plehn considered them related to malaria.

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[1] Read by Dr. Alfred Stengel at the Sixteenth Annual Meeting of the Association of American Physicians, held at Washington, D. C., April 30 to May 2, 1901.

Grawitz, in his paper of September, 1899, was the first to lay particular stress on this granulated cell as an evidence of a special form of degeneration, and he opposed the earlier view of fragmentation or persistence of remnants of the nucleus, and pointed out that in his observations these cells were found in blood in which there was no other evidence of cellular change, and in which there were no nucleated erythrocytes; and, further, that when nucleated cells were present there were no transitional stages. Later, he demonstrated that this degeneration could be seen in nucleated cells while the nucleus was intact. In further studying the cells of the blood-forming organs he was unable to find this change in the newly-formed cells or in the erythroblasts, and, therefore, came to the conclusion that this degeneration was probably of peripheral origin, and he suggested that it was possibly due to the direct action of some blood poison. Litten substantiated this view in the study of the bone-marrow in cases of severe anæmias, where he found much evidence of erythrocytic degeneration, but was unable to find evidence of this special granulation. On the other hand, both Pappenheim and C. S. Engel have seen similar granules in embryonal blood. Hamel and Behrendt were the first to demonstrate the frequency of this cellular change in the peripheral blood of patients poisoned by lead. These observations gave Grawitz support for his former theories regarding their origin, and led him to study the blood under experimental intoxications with this metal. Experimentally he was able to observe these granulated cells in the blood of mice at a very early stage of the intoxication, and even when these animals had been subjected to the minute dose of 0.03 gramme of the acetate of lead for a very short time. Moritz repeated similar experiments, using rabbits, and clearly demonstrated to his own mind that these granulations are an evidence of a true degeneration and not artefacts.

Sabrazès, Bourret, and Léger claim to have first produced these granules experimentally in animals, using guinea-pigs and injecting small doses intraperitoneally.

Grawitz, working upon a theory suggested by Plehn's observation of similar granulations in the blood of Europeans coming to the tropics, thought that the change of temperature had something to do with their formation. Following this idea, he was able to demonstrate the presence of these granules in mice subjected to increasing daily temperatures.

Schur and Loewy, in an extensive study of the bone-marrow in various diseased conditions, were unable to find such granulations. They came rather hastily to the conclusion, therefore, that this cellular condition was of artificial production.

From the foregoing observations and experimental studies it seems to us without a doubt that these granular formations, be they the remains of fragmentation of a previously existing nucleus or a special production, are an evidence of a pathological change when found in the circulation. With this in mind we have undertaken the study of this granular degeneration in lead workers and experimentally in its relations to lead intoxications. Our studies have included :

1. Cases of chronic lead-poisoning.
2. Studies in lead workers with no subjective symptoms.
3. Heat cases—heat workers and local therapeutical heat applications.
4. Results of experiments.

1. *The Cases of Chronic Lead Intoxication.* In all the cases so far reported by Hamel, Behrendt, Grawitz, Moritz, etc., in which the granules have been sought they have invariably been found. This granular formation seems to be a very early evidence of lead intoxication ; in fact, as will be seen later, appearing before all other symptoms, considered subjectively or objectively. The number of granular cells appears to be in direct proportion to the severity of the poisoning, and their disappearance is noted as the symptoms ameliorate.

Four of our cases were hospital cases, the men coming under observation with marked and typical symptoms of chronic poisoning. The granules were present in all four cases in varying numbers up to nine in one field (of a very thin spread and $\frac{1}{12}$ oil immersion). The granules varied in size, some cells showing very fine and others very coarse granules, and others a mixture of both. It might be said that in the severest cases the coarser granules are slightly in excess.

The blood otherwise showed only very slight changes from normal, namely, a slight paleness of the erythrocytes, and a slight poikilocytosis, especially marked in irregularity of size. A very few nucleated erythrocytes were seen. These were normoblasts, and the majority of them showed the granular degeneration of their protoplasm while the nuclei were intact as far as could be detected.

2. *Lead Workers Without Subjective Symptoms.* Grawitz and Moritz each had five cases which could be included under this head, and in which they found granules. Examining twenty-one lead workers without subjective symptoms we found the granules present in every case. The spreads of blood were taken at the workshop while the men were actually engaged at their various duties. The nature of the work of these men included that of foreman of the works, " sprinklers " who watered the dust, and laborers, some handling the metallic lead, others

the oxide, others the " wet pulp." These men were more or less exposed to the dust of lead during their working hours.

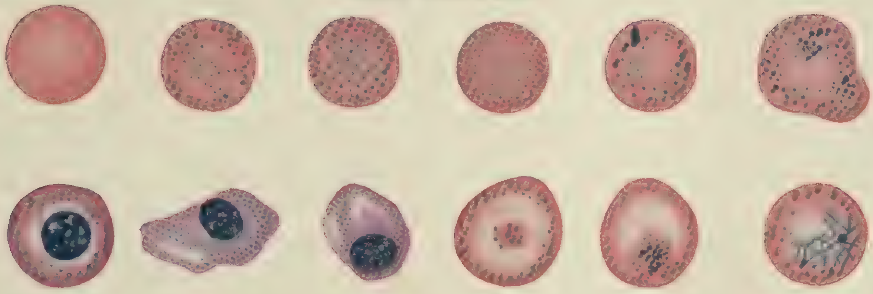
The list includes two who had worked only four days, the shortest exposure, and one man who had been constantly working in the metal for twenty-four years, the longest exposure. Only one of the twenty-one men, an oxide worker, had presented symptoms. This one had had several distinct attacks of chronic lead-poisoning in ten years of actual contact with the metal. One other, who had been working only three months, and who showed the greatest number of granules in the stained spread, had had about one month previous to observation an indefinite illness which had detained him one week from his work. The number of these granulated cells varied from a few in a spread to as many as two or three in a field of the microscope. The other evidences of blood changes were only slight and rather inconstant as to any particular form of variation. Twelve cases showed slight poikilocytosis, but more particularly irregularity in size of the corpuscles. Two at least certainly had deficient hæmoglobin (noted by the lack of stain taken by the cell). Three showed only a slight polychromatophilia, and in five cases normoblasts were observed, most of these latter cells showing granules in their protoplasm while the nucleus was unchanged. (See table at end of article.)

3. *Heat Cases.* The studies we made in this line were suggested by Grawitz's experiments with mice and by Plehn's observation on Europeans coming to the tropics, and by a case of an iron worker in whose blood we had found granulated cells in large numbers. They consisted in studying the blood of four iron workers who were subjected to intense heat while at their work at furnaces, and that of patients using local dry hot air treatment. In these latter cases, of which there were four, the various parts of the body, especially the limbs, were subjected to a temperature of 300° F. In the former as well as in the latter cases we were unable to find a single granulated cell in the spreads made from the peripheral circulation.

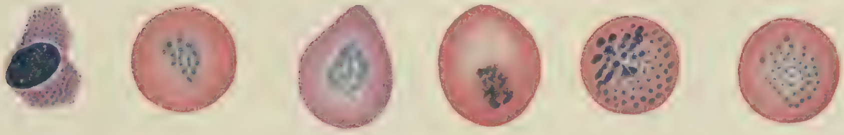
In the case above mentioned we were led to conclude that the granules were the result of the chronic diarrhœa which had existed for twenty years, or were possibly due to lead which he not unlikely received during a prolonged course of treatment. Here we might include five cases which had been subjected to applications of lead-water and laudanum. In two of these cases the application had been made to denuded areas, while in the remaining three to the unbroken skin. Daily observations were made in these cases for a week or ten days, but in them we were unable to find any evidence of granular degeneration.

4. *The Experimental Study.* These granules have been produced in mice by Grawitz, in rabbits by Moritz, and also in guinea-pigs and pigeons by Sabrazès, Bourret, and Léger.

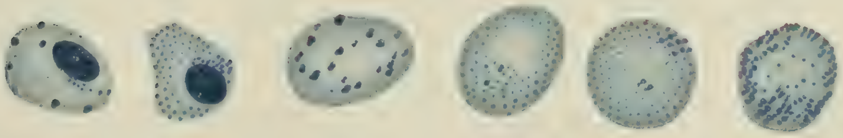
Lead Workers.



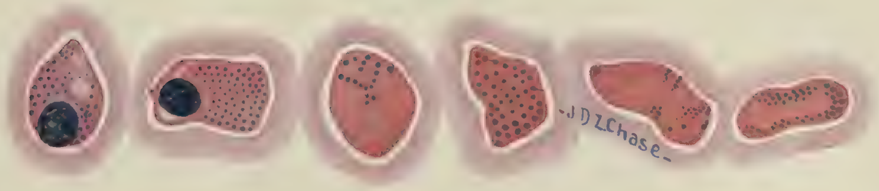
Dog's Blood.



Lead Poisoning.



Bone Marrow.



STAINS.—Nos. I., II., and IV., Eosin and Hæmatoxylin. No. III., Thionin Phenique.

In our own cases dogs were used, and the lead acetate was administered by mouth in capsules with the food. The initial dose was always a gramme, irrespective of the animal's weight. In two dogs one gramme was given daily throughout the observation; in three the initial dose of one gramme was increased by one gramme each day until the experiment was concluded. The blood in all these cases was carefully studied for several days previous to the experiment, and then every twenty-four hours for a few days after the intoxication had begun, and then at longer intervals. Spreads were made from the carefully shaven and cleaned ear, dried for twenty-four hours, and then fixed by heat, and studied under various stains.

Distinct granules appeared after the initial dose, usually in about three days, irrespective of the size of the dose compared to the animal's weight, or to the manner of increase of the same, though indistinct granules were noted after twenty-four hours. In the three cases in which the dose was rapidly increased the granules became more numerous in a shorter time than when the gramme dose was given daily. In all of these cases the early granules showed a greater tendency to cling together than they did later. This clinging together or clumping of the granules in different parts of the cell was more or less characteristic in these experimental productions. It was usually absent in the cases of lead-poisoning or of the lead workers. On the other hand, the even distribution so commonly seen in the lead workers was not observed at any stage of the experimentally produced poisonings. In the dogs it was a common observation to find associated with these granulated cells erythroblasts and polychromatophilia. The finding of these latter types of blood degeneration does not seem to us to be of such significance as when they are found in the human subject. They are a rather frequent finding in dogs which are used for experimental purposes. The appearance of granular degeneration in the peripheral blood, twenty-five hours after one of the writers had taken seven and one-half grains of lead acetate, shows conclusively the early production of this change in human blood.

The fact that these granules were not found in the bone-marrow by the various observers led us to believe with Grawitz that they were of peripheral origin, or that the usual methods for fixing the bone-marrow were inadequate for their demonstration. To determine the former view blood was taken from various veins of the body, stomach, mesentery, liver, portal vein, spleen, and heart in animals killed for this study, and compared with the blood taken ante-mortem from the ear. The results of these observations were as follows: The blood taken from the portal vein and splenic vein showed a greater number of these granules than did the blood of the ear, heart, or mesenteric vessels. This was but an isolated observation, and we hesitate to draw any definite conclusions. In five later cases this unequal distribution was not sufficiently marked to prove the peripheral origin of these granules.

For the study of the bone-marrow two methods were used. The bone was sectioned in pieces, three-quarters of an inch long, and the marrow was taken from its bony case by running an ordinary sewing needle around it, then, when it was freed from the bone, carefully pushing it out. In this way the marrow was obtained intact. Spreads were made from this marrow by the usual methods for making blood smears. Some of these spreads were fixed immediately in ether and absolute alcohol; absolute alcohol; 10 per cent. formol; saturated aqueous solution of bichloride of mercury; 1 per cent. osmic acid; saturated solution of picric acid in absolute alcohol; others were dried and fixed with heat alone, or previously to heating treated with ether to remove the fat. Further, this shelled-out bone-marrow was fixed by the usual methods and sections made from paraffin blocks. From the former spread specimens, variously fixed, we were able to demonstrate the granular changes in the erythrocytes and the erythroblasts, but in no bone-marrow spread was the number of these granules in greater number than we found in the peripheral circulation. These cells may have been in the circulation of the bone-marrow. The fixing agents from which the best results were obtained were ether and absolute alcohol, absolute alcohol, and bichloride solution. From the great amount of fat which is always present in these spreads, and which interferes to a great extent with fixing the specimens by the usual heat method, it was thought that it might interfere with the staining of these granules. To ascertain the rôle which fat played in this way spreads from the ear blood were kept at 52° C. for twenty-four hours on fat taken from the mesentery of a dog. They were then fixed by heat and stained in the usual way. While the granules could be found after the spreads were so treated there seemed a decrease in their number, especially so in the case of the finer granules.

From the bone-marrow fixed in the various methods and mounted in paraffin sections were cut at 2μ. In these sections fixed by various agents—alcohol and ether; absolute alcohol; osmic acid, 1 per cent.; formol, 10 per cent.; Müller-formol; Zenker's solution; Flemming's fluid—we were unable to demonstrate the presence of granules.

In our routine study of these granulated cells all the blood spreads have been fixed by heat on a copper plate. The specimens heated for a few minutes only seem to be better prepared for staining than those heated for a longer time. The stains used for this work have been the usual hæmatoxylin and eosin stains and thionin phéniqué. In using the former stains the specimens should be overstained with hæmatoxylin; with the latter the granulated cells stain rapidly and are very easily detected.

With aqueous solutions of the following stains we have been able to detect these granules in specimens fixed by heat: basic fuchsin, carbol-thionin, aniline green, gentian violet, Bismarck brown, tuloidin-blue, dahlia, methylene-blue; also Löffler's methylene-blue, hæmatoxylin, hæmalaum. We have been unable to find them when we used aqueous solutions of aniline blue, Berlin blue, Jod. green, indulin, tropæolin, blue-black, methylene-green, orange G., acid fuchsin, rosin, Ehrlich triacid, nile blue, benzopurpin. For routine work we recommend the use of the usual hæmatoxylin and eosin stains, or, which is especially good for the study of these granules, the thionin pheniqué, the formula of which is:

Thionin (French)	0.05
Carbolic acid	1.00
Alcohol 95 per cent.	10.00
Aq. destil.	90.00

The stain becomes better with age.

Our conclusions are:

1. The granules are a constant finding in cases of lead-poisoning, and appear very early in cases under the influence of lead salts long before subjective or other objective symptoms can be demonstrated.

2. The granules disappear in cases of chronic lead-poisoning as the convalescence is established.

3. Apparently lead does not produce an immunity, as one of the cases worked for twenty-four years, another for twenty years, without having pronounced symptoms of lead-poisoning, and in both of these cases the granules were present in moderate numbers.

4. The granules may be produced experimentally in dogs, appearing in a very few days after the beginning of the experiment, and increasing as the intoxication becomes severe.

5. The granules in the experimental cases are rather fine, and show a tendency to clump at first; later all varieties appear.

6. We believe these granules to be a true degeneration of the erythrocyte and having no relation to nuclear fragmentation or to polychromatophilia.

LEAD WORKERS.

Case No.	Time worked in lead.	Degree of exposure.	Poikilocytosis.	Hæmoglobin estimated by the amount of stain per cell.	Nucleated erythrocytes.	Granular degeneration.	Estimated average number of granular cells to a field ($^{1}/_{12}$ oil immersion).
1	7 years	Considerable.	Slight.	Normal.	Present (one in slide).	Present.	One to two cells to a field.
2	5 "	Moderate.	"	"	Absent.	"	One cell to every two or three fields
3	3½ "	Considerable.	"	"	Present (few).	"	One cell to every four or five fields.
4	24 "	Constant.	"	"	Absent.	"	One cell to every three or four fields.
5	7 "	Considerable; poisoning 5 yrs. ago.	Absent.	"	"	"	One cell to every ten or twelve fields.
6	9 "	Slight.	"	"	"	"	One cell to every ten or twelve fields.
7	11 "	Considerable.	Slight.	Reduced.	"	"	One cell to every ten or twelve fields.
8	9 "	"	Absent.	Normal.	"	"	One cell to every seven or eight fields.
9	7 "	"	"	"	"	"	One cell to every four or five fields.
10	2 wks	"	"	"	"	"	One cell to every six or seven fields.
11	6 "	Constant.	Slight.	Reduced, and polychromatophilia.	Present (many).	"	One cell to every six or seven fields.
12	8 mos.	"	"	"	Present (few).	"	One cell to every six or seven fields.
13	3 "	"	"	"	Present (many).	"	Two to three cells to every field.
14	4 days.	"	Absent.	Normal.	Absent.	"	One cell to every four or five fields.
15	4 "	"	"	"	"	"	One cell to every four or five fields.
16	5 years	Considerable.	Slight.	"	"	"	One cell to every field.
17	1 year	"	Absent.	"	"	"	One cell to every four or five fields.
18	2 wks.	"	"	"	"	"	One cell to every two or three fields.
19	4 "	Constant.	Slight.	"	"	"	One cell to every three or four fields.
20	20 years	Considerable.	Absent.	Reduced.	"	"	One cell to each field.
21	10 "	"	Slight.	Normal.	"	"	One cell to every three or four fields.

Extracted from The American Journal of the Medical Sciences, March, 1901.

A STUDY OF CONGENITAL SARCOMA OF THE LIVER AND SUPRARENAL.

WITH REPORT OF A CASE.

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(*From the William Pepper Laboratory of Clinical Medicine.*)

Case I.—B. L., a female child, was a private patient of Dr. McCreight, to whom, with Dr. J. H. McKee, I am indebted for this history.

Family History. Maternal grandmother died of dropsy, and grandfather of paralysis. Paternal grandmother living and well; the grandfather died suddenly of kidney trouble. The husband was insane seven years ago; was jealous of his wife; has not, however, been violent since, although occasionally has visual hallucinations. He denies any syphilitic infection. The mother suffers only from indigestion; has had seven children, only one of whom, a six-months baby, has died.

Previous and Present History. Born August 19, 1900. She seemed perfectly well until September 14th. Mother then noticed protruding navel. The next day the abdomen appeared large and shiny. Since then the abdomen has grown rapidly. The baby has lost some flesh and drinks a great deal. No appreciable fever. Bowels are loose and green in color. She seems to have some colic at times. Dr. McCreight first saw the child when it was four weeks old, and states that the abdomen increased visibly from day to day until death.

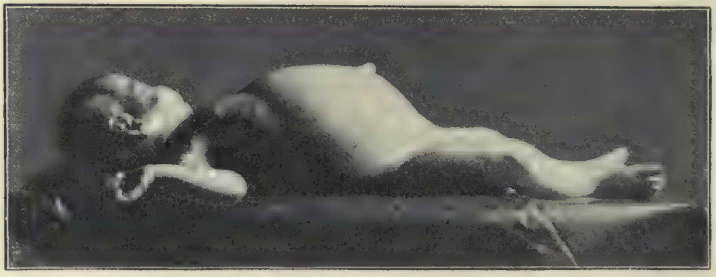
At an examination made on September 27th, when the child was five weeks old, the following notes were made:

Inspection. Much distended abdomen, almost symmetrical in character. Pouting umbilicus. Enlarged superficial veins. Marked bulging in both lumbar regions posteriorly, but especially on the right side.

Palpation. The abdomen is very tense anteriorly, and from the costal border to about one inch below the umbilicus in the median line gives the sensation of a firm, heavy, resistant growth. Below this point there is gurgling in the bowel on pressure. In the right iliac fossa the growth fills the whole area. Palpation readily indicates a sharp border, almost unquestionably liver, and slightly to the left of the umbilicus is found a distinct notch. This border dips deeply into the right iliac fossa. The mass is lifted markedly by deep pressure in either renal region, but the greatest sense of resistance is experienced in the right lumbar region posteriorly.

Percussion. The hepatic dulness does not extend above the level of the right costal border anteriorly. From the border down to below the umbilicus in the median line, and almost to Poupart's ligament in the right iliac fossa, there is absolute flatness. Posteriorly in the prone position there is absolute flatness in the right lumbar region and colic tympany over the left side.

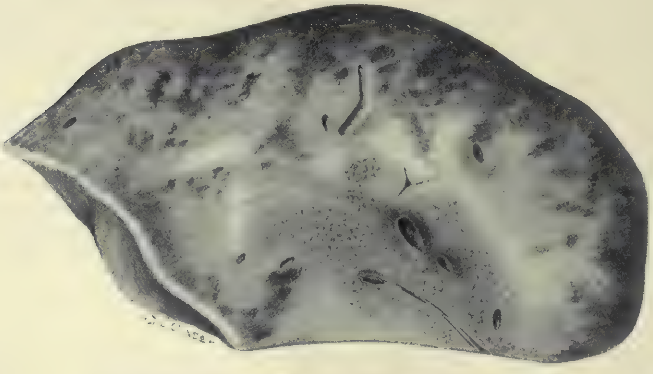
FIG. 1.



From a photograph taken after death.

The child died in convulsions on October 3, 1900, aged six and a half weeks. It had nursed until the last day. The body had wasted but very little, and the abdomen had grown so tense that the skin could not be pinched between the fingers. A few small hemorrhagic petechiæ had formed in either lumbar region a few days before death.

FIG. 2.

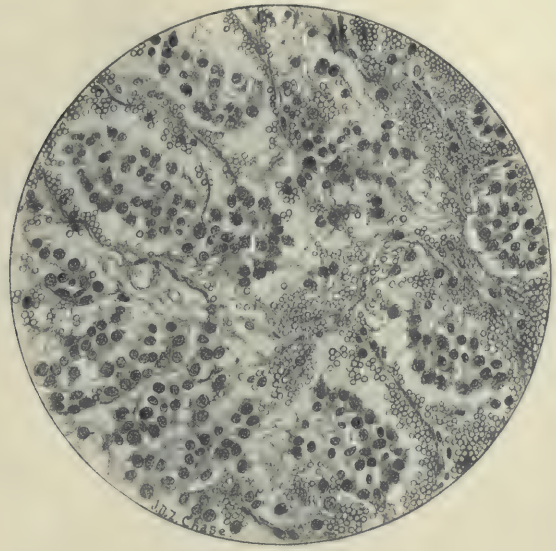


Appearance of the surface of a fresh section of the liver.

Post-mortem was performed by Dr. J. C. Gittings, at that time pathologist to St. Christopher's Hospital. The specimens were given to me for examination, as Dr. Gittings left the city in a few days.

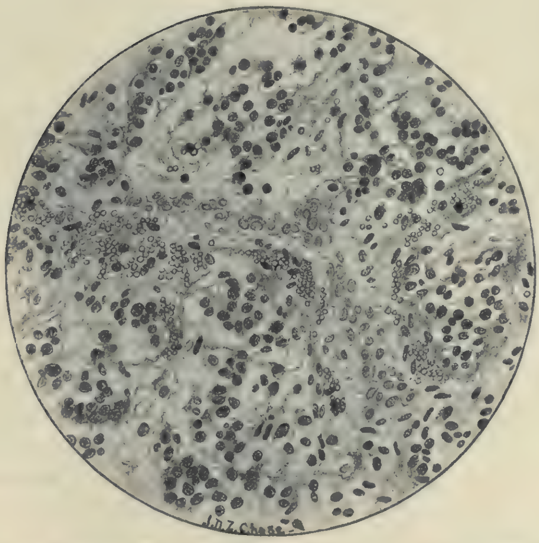
Body of a female infant, aged six and a half weeks. Well nourished; no eruption; no excoriation or redness around mouth, nose, or anus; no jaundice; no enlarged lymphatics. Protruding abdomen, with pouting umbilicus. The abdomen was completely filled by the

FIG. 3.



Section of suprarenal body.

FIG. 4.



Section of liver, showing infiltrating tumor cells and a band of compressed liver cells.

liver, which was seen to be much enlarged and bulged out below the costal margin and extended down almost to the symphysis. A minute quantity of serous fluid free in the peritoneal cavity. Lungs crepitant throughout, but congested. Heart normal. Spleen small, dark brown, and soft. Kidneys normal. Left suprarenal normal. Right suprarenal enlarged to the size of an English walnut, firm, and hemorrhagic in appearance. On section the surface presented a yellowish-white, homogeneous character, with scattered areas of hemorrhage. There were no abnormal adhesions. The liver weighed two pounds and eight ounces; was uniformly enlarged in all its lobes; no irregularities or nodules. The increasing convexity of the right lobe had caused the liver to slip out from beneath the costal margin. The capsule was smooth and glistening, with reddish and yellowish areas, giving it a mottled or marbled appearance. On section it presented a uniform yellowish-white appearance with small, hemorrhagic areas, and resembled the growth in the suprarenal, though it was not so distinctly hemorrhagic. The appearance suggested a diffuse neoplastic infiltration or a massive transformation. It was with difficulty that one could find any normal hepatic tissue showing acini. There were a few enlarged mesenteric glands, but these were not the seat of any growth.

Microscopical examination was made of sections from lungs, spleen, kidneys, and lymphatic glands, all of which were normal. The study of sections from the growth in the right suprarenal showed that there was still a remnant of the gland left at the periphery of the mass. The tumor was a typical lymphosarcoma, and, stained with van Giesen's method, showed a small amount of fibrous connective tissue in an alveolar arrangement, filled with masses of loosely packed, round, lymphoid cells, about twice the size of a red corpuscle. The growth was very hemorrhagic, and the blood was not confined to the vessels, but was free throughout the tissue. Sections from various portions of the liver showed the same lymphosarcomatous growth, though less hemorrhagic, and in places small islets of liver cells surrounded and infiltrated by the growth or compressed and squeezed into narrow bands. In no place could a typical secondary nodule be found surrounded by liver tissue, because the remnants of liver structure were so small and so surrounded by the growth that such a condition was impossible. The amount of fibrous connective tissue was not prominent in any portion of the tumor, being always subordinate to the number of lymphoid cells.

A very careful review of the literature upon the subject of primary sarcoma of the suprarenal and of the same in the liver was intensely interesting, because I found five cases of such striking similarity to the one I have just reported that I have thought it important to abstract them quite fully, to show that we have here a special type of congenital malignant disease, with its own peculiar symptoms and pathological findings.

CASE II. *Congenital round-celled sarcoma of the liver.*—George Heaton (*Transactions of the Pathological Society of London,* 1897–98, vol. xlix., p. 140). The patient, a girl, aged eight weeks, was admitted into the Children's Hospital, Birmingham, with a history of rapid abdominal enlargement, with general wasting. The abdomen was noticed at birth to be unduly prominent, and this prominence increased rapidly until admission a few days before death. During a week while the child was under observation the abdomen increased in circumference one and a half inches. It was distended by a tumor occupying the epigastric, the right and left hypochondriac regions, descending downward below the umbilicus. The tumor had the characteristic signs of an enlarged liver. There was no jaundice and no ascites. The mother and father were in every way healthy. There were two other children alive and well. There was no evidence whatever of any syphilitic taint. The child sank gradually, and died aged nine weeks.

Post-mortem Examination. There was much general wasting of the body. The abdomen was distended by a uniform swelling occupying the position of the liver and extending considerably below the level of the umbilicus. The spleen was of average size and showed no lesion. The kidneys were anæmic. There was no enlargement of any of the abdominal lymphatic glands nor any evidence of old or recent peritonitis. The right suprarenal capsule was enlarged by a nodule about the size of a marble, occupying its posterior half. On section it was dark red. The left suprarenal capsule showed no abnormality. The liver was greatly enlarged and weighed forty-nine ounces. The enlargement was uniform, all its lobes being equally affected. The surface was smooth and glistening, the peritoneal coat being normal in appearance, and there was no thickening of the capsule. In the fresh state the surface had a most peculiar mottled or marbled appearance, being covered with numerous red patches, separated from one another by pale, dull areas. A section of the liver presented the same appearance. There were numerous patches of a dark red color surrounded by zones of a lighter color. The gall-bladder was contracted and empty. The sulcus in which it lay did not nearly reach the free margin of the organ, indicating a rapid enlargement of the organ in a downward direction. Microscopical examination of the enlarged liver showed: 1. Areas in which there was considerable vascular enlargement corresponding to the dark red patches seen with the naked eye. 2. Liver cells showing apparently no change. 3. Areas of small cell growth corresponding to the pale patches seen by the naked eye. These areas contained large numbers of round cells, fairly uniform in size and rather densely packed together. At the margin of these areas the cells were seen infiltrating between the liver cells, even extending some distance away from the main collection. Where this infiltration was taking place the liver cells showed a considerable amount of alteration, being atrophied and in many instances so changed that their distinctive characters were lost, and they appeared as irregular atrophied cells. The organ would, therefore, appear to have been the seat of a diffuse round-cell sarcoma which had begun primarily within its substance during intra-uterine life and caused a rapid, uniform enlargement, with partial disappearance and destruction of the liver cells. The diagnosis of sarcoma is supported by the great and rapid enlargement of the organ, the absence of any enlargement of the spleen or lymphatic glands, and the presence of a secondary nodule of an exactly similar character in the right suprarenal body.

Case III. *Sarcoma of suprarenal capsules in a child, aged seven weeks.* —John Orr (*Edinburgh Medical Journal*, September, 1900) reports the case of a female child, aged seven weeks, brought to the dispensary on account of " swelling of the belly." The history given was that the infant was born at term at a maternity hospital, apparently normal, and no evidence of disease detected by the physician in charge. A fortnight before the child came under Dr. Orr's care the mother had noticed that the abdomen was unduly prominent and was increasing gradually. The child otherwise seemed well and took nourishment naturally. It was the youngest of a family of eight, who, except the fourth, an imbecile, were born healthy and have remained so. The only constitutional taint on either side of the family was an old tubercular knee-joint of the father. The child suffered no pain, and was well nourished and showed no discoloration or pigmentation of the skin. On examination the following was noted : The superficial abdominal veins were distended, especially in the upper part. Palpation over the distended upper abdomen revealed what was taken to be an enlarged liver and spleen, extending to a little below the umbilicus. Both these swellings were perfectly smooth and uniform. Circumference just above the navel, the most prominent part, was seventeen and one-half inches. No glandular enlargements. The blood showed at first a leucocytosis, which later disappeared. The child lost weight and the abdomen increased in girth, and the two areas of enlargement and dulness descended into the right and left iliac fossæ respectively. The circumference became nineteen and one-half inches. The child weighed eleven pounds and three ounces. Death occurred nine weeks after the case came under Dr. Orr's care, the child then being four months old. Various diagnoses were discussed. The post-mortem showed, however, that the supposed enlarged spleen was an enlarged left lobe of the liver and that the spleen was normal. The enormous hepatic enlargement was sarcomatous, and the primary seat was in the right suprarenal. Both lobes of the liver were uniformly enlarged. The surface was perfectly smooth, but showed shining through its capsule, which was in no way thickened, a large number of small, white areas, mostly circular, though occasionally irregular, from confluence. The liver weighed just under three pounds. On section these nodules were still more evident. They were of a whitish or yellowish-white color, with hemorrhagic foci here and there. They infiltrated the liver everywhere. All the other organs were healthy except the two suprarenal bodies. In place of the right one there was a large growth, weight seven ounces, which almost hid the kidney from view. The growth was roughly globular, and was surrounded by a firm, fibrous capsule, and there were no firm adhesions. It was soft, of a dark red color like a blood clot, and was spotted with white. It showed no recognizable suprarenal tissue. The left suprarenal had preserved its shape, though enlarged and infiltrated with whitish-yellow nodules of secondary growth. Microscopical examination of pieces of the primary and secondary growths was made, and it was found to be mainly a cellular growth, the cells being chiefly round and averaging from 8 to 10 mm. in diameter, each with a large, deeply staining nucleus and a comparatively thin rim of protoplasm. It was highly vascular. In some few places it was more fibrous, probably older areas. In the latter the fibrous tissue was collected in fairly well-formed alveoli in which the cells lay. Orr calls attention to the peculiarly smooth, uniform character of the secondary hepatic enlargement.

CASE IV. *Diffuse sarcoma of the liver, probably congenital.*—R. W. Parker (*Transactions of the Pathological Society of London*, 1880, vol. xxxi.) reports a case of a female child, seen at the age of three weeks on account of swelling and hardness of the abdomen. There had been no jaundice. The child was emaciated, the abdomen distended and in the region of the liver uneven, and there were a few enlarged veins ramifying over it. A hard mass was felt extending from one side to the other and down to the iliac crests. Mercurial inunctions failed to produce any improvement. The child died at the age of five weeks. A partial autopsy was made. Body was much emaciated. Bones appeared normal. Liver filled the abdominal cavity almost entirely. Weighed thirty-two ounces. When first removed it was of a dark plum color, mottled over with patches of a yellowish tint, corresponding, when cut into, to a new growth, which was largely diffused through the whole liver. This dark color quickly changed to a bright scarlet after removal of the liver from the body. It was obviously due to the presence of blood, with which the organ was distended. The new growth was scattered throughout the entire gland as nodules varying in size from a millet-seed to a walnut. It looked not unlike caseous material, but it could not be shelled out from the liver substance. The surface of the organ was slightly nodulated, its capsule shiny and not thickened. Left lobe was as large as the right. From the lower surface several nodules projected. Gall-bladder rudimentary, kidneys normal, also spleen. There was a mass of new growth between the spleen and left kidney as large as a Tangiers orange. This was the only secondary growth; it was very vascular and soft. Microscopical examination of the liver tumor showed that it was mainly composed of round cells, larger than red blood-corpuscles. The proper gland cells of the liver could not be found in the many sections examined. Even in places where there was no obvious naked-eye change the liver substance was infiltrated with a dense, small cell deposit which quite obscured the liver cells even if they were present. Some areas showed extravasated blood. At the periphery there was an abortive appearance of portal zones. Dr. Parker called this growth a congenital round-celled sarcoma, and rejected the possibility of its being syphilitic.

CASE V. *Congenital tumor of the liver and both suprarenals.*—De Ruyter (*Langenbeck's Archives*, 1890, vol. xl., p. 98) reports the case of a infant whose parents noticed almost immediately after its birth that the abdomen was enlarged and that it was increasing in size from day to day. On the fifth day the child was brought to the clinic; it showed then no abnormalities except enormous distention of the abdomen. Congestion of the veins over this area was marked. The greatest circumference was in the neighborhood of the navel, and was 55 cm. Palpation revealed throughout the whole abdomen an equally elastic resistance. This mass was everywhere smooth and free from inequalities. *Clinical diagnosis.* Suprarenal tumor. For three days the child took a fair quantity of milk, but on the fourth and fifth days refused nourishment. The breathing became more superficial on account of increase in the size of the abdomen. Extensive cyanosis appeared and death followed. *Post-mortem.* Emaciation quite advanced. On opening the abdomen all the organs were hidden by a tumor extending from the costal border to the symphysis. This tumor had preserved the exact form of the liver in which it had developed. The surface was smooth, without any depressions or elevations. There were no adhesions. Spleen normal in size and structure. Occupying the position of the left suprarenal was found a tumor the size of an apple adherent to the kidney, although easily separated from it. Both kidneys were normal. Section of the left suprarenal tumor showed alternate darker and lighter layers. Macroscopically nothing of the suprarenal tissue could be seen. The right suprarenal was half as large as the left and very hemorrhagic. The liver, or, more properly speaking, the liver tumor, was 20 cm. broad, 12.5 cm. high, and 6.5 cm. thick. The whole organ was enlarged proportionately. The capsule was moist, smooth, and glistening, and through it shone a yellow, speckled, brownish-red tissue. The gall-bladder, having retained its normal size, was fully covered by the growth of the right lobe. Section through the liver tumor showed it to be very rich in blood, and that it was made up of a partly yellowish and partly grayish-red marbled tissue of such indistinct composition that the acinous liver tissue could be no longer detected. Microscopical examination of the liver tumor showed that of the original liver tissue practically nothing remained, but in its place throughout the whole mass was a structure composed of an alveolar framework of connective tissue filled with round cells. The connective tissue was rich in bloodvessels. In a few places were some irregular shaped multinucleated cells, which were thought to have been remnants of the old liver cells. Section of the left suprarenal tumor showed the same condition, except that in one part the cortex of the old suprarenal was still present. The right suprarenal was also involved in the same manner, but was much more hemorrhagic; in fact, a telangiectatic condition was present. Dr. O. Israel examined sections microscopically from the liver tumor and the suprarenals, and diagnosed those from the liver and right suprarenal as congenital lymphosarcoma and those from the left suprarenal as hemorrhagic telangiectic lymphosarcoma.

CASE. VI. *Myxosarcoma of the liver in an infant aged four months.*—Meisenbach (*Weekly Medical Review*, St. Louis, 1884, ix., 433). Female child, apparently normal at birth. About two weeks later the mother noticed a swollen condition of the abdomen, and the navel protruded, teat-like. There is no history of any specific disease. Dr. M. saw the child at the age of eleven weeks. Restless, vomited milk, but nursed pretty well. Abdomen excessively and symmetrically enlarged; the abdominal veins congested, navel protruding. Percussion gave complete dulness extending from the xiphoid cartilage downward into the hypogastric regions, and latterly posteriorly into the lumbar and iliac regions. Palpation detected a firm, smooth, resisting mass filling the entire abdominal cavity, with the exception of a small space in the hypogastric region, where, on deep pressure, the free margin of a firm body could be felt. The child was put on antisyphilitic treatment, with apparently slight decrease in the size of the liver. Died aged sixteen weeks. Abdomen was seventeen inches in circumference. Navel protruding, but flabby. Small amount of fluid in the abdominal cavity.

Liver enlarged, filling entire abdominal cavity, bulging up under the xiphoid cartilage, with inferior margin in the hypogastric region. Liver presented smooth, symmetrical enlargement, color mottled, like red castile soap. Spleen and kidneys normal in size, but also mottled.

There is a remarkable resemblance between these six cases, and in order to make this more apparent I shall tabulate the points of similarity.

1. The age at which the first symptom—swelling of the abdomen—was observed was: In Case II. at birth; in Case V. almost immediately after birth; in Case VI. two weeks; in Case IV. three weeks; in Case I. between three and four weeks, and in Case III. five weeks. This seems to prove that these six cases were certainly all congenital, especially when the extensive involvement of the liver is considered.

2. The age at which the children died was as follows: Case V. lived ten days; Case IV. lived five weeks; Case I. lived six weeks; Case II. lived nine weeks, and Case III. and Case VI. lived sixteen weeks. This shows the great malignancy of these growths.

3. The rapidity of growth of these tumors is shown by the fact that in Case V. a difference could be noted from day to day, and the circumference reached 21.7 inches. Case II. grew rapidly until it came under close observation, and then in one week the abdomen increased one and a half inches; the liver weighed forty-nine ounces. Case I. grew very rapidly, and the liver weighed forty ounces. Case III. grew more gradually, and while under observation increased two inches in nine weeks, and the liver weighed forty-eight ounces. In Case IV. it is not stated how rapidly the abdomen increased, but the liver weighed thirty-two ounces. In Case VI. it is supposed to have decreased slightly, but at death the abdomen measured seventeen inches.

4. The sex of Case V. is not mentioned; all the others were females.

5. Clinical symptoms: Distention of the abdomen was present in all. Wasting was present in varying degrees, although it does not seem to have been as extreme as one might have supposed would have occurred. Ascites is not noted in any case, nor is jaundice or any form of pigmentation of the skin. The children all nursed well until shortly before death. There does not seem to have been much pain, nor is there any mention of a rise of temperature. There was no syphilitic history in any of them, nor were any signs of syphilis found.

6. The growth in the liver in these cases was identical in its appearance and showed the same equally infiltrative proliferation by the sarcomatous tissue, with practically complete destruction of the entire normal liver structure.

7. The growth in the suprarenals exhibited the peculiarity of being very hemorrhagic. In Case II. there was a nodule the size of a marble

in the posterior half of the gland. In Case III. there was a mass the size of an apple in the right, and none of the normal tissue remained. The left was also enlarged and infiltrated with small nodules. In Case V. the left was replaced by a tumor the size of an apple, with complete destruction of normal tissue, and the right was half as large. In Case I. the right was as large as a walnut, and the cortical layer of the suprarenal gland still remained around the periphery of the growth. In Case IV. there was a mass of new growth lying between the spleen and the left kidney. (May this not have been the left suprarenal gland, especially since the autopsy is described as being only partial and the suprarenals are not even mentioned?) In Case VI. the suprarenals are also not mentioned. This case is, however, not very fully reported.

8. In all these cases no other organ or part of the body was involved by the new growth.

9. The pathological diagnosis in Case IV. was round-celled sarcoma, the same in Case II. and Case III. In Case VI. myxosarcoma; in Case V. lymphosarcoma, and also in Case I.

10. The primary seat was thought in Cases II., IV., and VI. to have been the liver. In Cases I. and III. the right suprarenal; in Case V. it was simply called a sarcoma of the liver and both suprarenals.

11. The absence of the following points in these cases differentiates them from a possible syphilitc affection of the liver and suprarenals: *a.* There was no overgrowth of connective tissue in any of the tumor masses. *b.* There was no amyloid change in any organ. *c.* There was no perihepatitis. *d.* There was no jaundice. *e.* There was no enlargement of the spleen. *f.* There was very little if any pain in the neighborhood of the liver. *g.* There was no nephritis. *h.* The markedly hemorrhagic condition of the tumors.

These six cases, beside showing such a similarity to one another, have another point of interest, namely, they are so dissimilar to all other reported cases of either primary sarcoma of the suprarenals or of the liver that I have tabulated forty-six cases of primary sarcoma of the suprarenal in addition to those abstracted above, which I have found in a thorough search through the literature. These cases occur in various periods of life. The earliest are one by Cohn, in a nine months' old girl, with a large growth in the left suprarenal and metastases in the skull, kidney, liver, ovary, and ribs; one by Pitt, in a ten months' old boy, with a tumor the size of a hen's egg in the right suprarenal, and a large nodule in the liver, which may have been the primary seat; one by Caillé, in an infant with a tumor in the left suprarenal and a diffuse secondary growth in the neighborhood of the third cervical vertebra; one by Dobbertin in a fourteen months' old girl, who had a growth in the abdomen since birth; an operation was performed, and the left kidney together with the growth were removed together. The diagnosis of sarcoma was not certain, however.

From these cases occurring in infancy others are found up to the two oldest, both sixty-eight years. None of these cases show this infiltrating character of the growth which was so characteristic of the cases that I have abstracted above in full, nor did any of them present the same clinical picture.

In looking over the literature of primary sarcoma of the liver I find few cases, and a number of these are rather doubtful. Among these cases the earliest was one reported by Pepper before the Pathological Society of Philadelphia, in 1873, as a case of primary carcinoma in a child, aged eight weeks. This case was quoted by Arnold and Birch-Hirschfeld as presumably a sarcoma. The growth was a circumscribed nodule in the left lobe of the liver. Gee (*St. Bartholomew's Hospital Reports*, 1873, vol. vii.) reports an early case in a child, aged five months, with countless nodules in the liver. West, quoted by Birch-Hirschfeld, reports another in a boy, aged nine months, with a tumor in the liver and metastases in the lung. Arnold and Birch-Hirschfeld also believe these to be sarcomas. Von Windrath (*Inaug. Dissert.*, Freiburg) reports another case occurring the first year of life, in which the liver, the only organ involved, was the seat of numerous various sized nodules, which were, however, sharply separated from the surrounding tissue.

PRIMARY SARCOMA OF THE SUPRARENAL GLAND.

No.		Sex and age.	Reference.	Clinical course.	Supra-renal; size, etc.	Metastases.	Variety of sarcoma.
1	Ermi quotes Doderlein	M. 47	Dissertation, Erlangen, 1860.	Skin gray; icteric, abdominal tumor.	Right, man's head.	None.	Sarcoma.
2	Kussmaul	M. 47	Wurz. med. Zeitschr., 1863, No. 24.	Cachexia, slightly icteric, mass felt in right hypochondrium.	Right, man's head.	None; only adhesions.	Melanotic sarcoma.
3	Greenhow	F. 12	Trans. Path. Soc. London, 1867, xviii.	No pain or wasting; pneumonia; no pigment.	.... 3×2 in.	None.	Sarcoma.
4	Coats	F. ...	Virchow, Hirsch. Jahr., 1872, i. p. 244.	....	Left, 18 lbs.	None.	Round & spindle-celled.
5	Eberth	F. $1^{5}/_{12}$	Virchow's Arch., 1872, lv. p. 518.	Mass felt in abdomen; ascites; diarrhœa.	Right.	Left kidney, peritoneum, and diaphragm.	Myosarcoma.
6	Smith	M. old man.	Dublin Journ. Med. Sci., 1877, lxiv. p. 555.	No pigment.	Right, 8×3½ in.	None.	Cystic sarcoma, round and spindle-cell.
7	West	M. 57	Path. Soc. Lond., 1878–79, vol. xxx.	Bloody sputum; wasting; no discolorat'n of skin; dulness over right lung.	Right, 5×4½×3 in.	Lung and bronchial glands.	Sarcoma.
8	Merkel	M. ...	Ziemssen's Handb. Spec. Path. u. Ther., 1875–80, Bd. viii. 2d half, p. 301.	Skin faint brown.	....	No secondary.	Sarcoma.
9	Rosenstein	M. 40	Virchow's Archiv, 1881, Bd. lxxxiv.	Pain; loss of appetite; tumor felt; urine normal.	Left, large.	Right suprarenal, kidney, pancreas, heart.	Small-cell sarcoma.
10	Fox	F. 2	Trans. Path. Soc. London, vol. xxxvi. 1885.	Rickety; dusky skin; hairy; abdomen enlarged gradually.	Left, cocoanut.	Lung.	Large-cell sarcoma.
11	Turner	M. 25	Ibid.	Horseshoe kidney.	Both.	Mediastinum involving lung.	Round-cell sarcoma.
12	White	...	Ibid., p. 464.	No pigmentation.	Left.	None.	Sarcoma.
13	Fränkel	F. 18	Virchow's Archiv., 1886, Bd. ciii. p. 244.	No pigment; nephritis; retinitis.	Left, fist; right, hazelnut.	In right suprarenal.	Angio-sarcoma.
14	Gade	M. 4	Förd, Norske med. Salsk. Kristiania, 1886.	Pain, emaciation, and abdominal tumor.	Both, in one mass, child's head.	Liver.	Round-cell sarcoma.
15	"	M. 6	Ibid.	Supposed to have psoitis or spondilitis.	Right, child's head.	Liver and right lung.	Round-cell sarcoma.
16	Perry	M. 23	British Med. Journ., 1888, vol. i. p. 1382.	Symptoms resembled Addison's disease.	Both, R. ¼ oz., L. 1 oz.	None.	Spindle-cell sarcoma.
17	Blackburn	M. 48	Journ. Amer. Med. Assoc., 1888, vol. x.	Chronic mania; pain; anæmia; not diagnosed.	Right, 97¼ oz. 8⅝×5⅞.	No secondary nodules adherent to adjacent organs.	Large-celled, round-cell sarcoma, cystic.
18	Pilliet	M. 56	Bull. de la Soc. Anatomique de Paris, 1888, p. 716.	Œdema; exhaustion.	Right, 25×20 cent.	Inferior vena cava, right auricle.	Sarcoma.
19	Griffiths	M. 41	British Med. Journ., Feb., 1889.	3 months sick; gangrene of left foot.	Both, 2×½	None.	Sarcoma.
20	Berdach	M. 55	Wien. med. Wochensch., 1889, xxxix.	Tumor felt, also superficial nodules; pain; skin slightly brown.	Left.	Liver, stomach by continuity, skin.	Small-celled, spindle-cell sarcoma.

No.		Sex and age.	Reference.	Clinical course.	Supra-renal; size, etc.	Metastases.	Variety of sarcoma.
21	De Paoli	M. adult	Per l XXV anno del insegnamento Chirurgico de Francesco Durante, 1889, i. 219.	Operation performed.	Right, man's head.	Liver, spleen, left suprarenal, kidney.	Sarcoma.
22	De Paoli	M. adult	Ibid.	Dyspnœa; subicteric.	Left, fœtal head.	Liver and lung.	Angio-sarcoma.
23	Orth	F. 58	Arbeiten aus dem path. Institut in Göttingen. R. Virchow, 50 z. Jubiläum, 1895.	……….. …	Left, fist.	Kidney, right suprarenal, pia mater, brain, lungs, liver, intestine, lymphatics.	Melan-sarcoma.
24	Lazarus	… 3½	Med. Press and Circ., London, May, 1894.	Pain; swelling; mass in abdomen, emaciation, while weight increases.	Left. 12 lbs.; child 37 lbs.	None.	Sarcoma.
25	Jores	M. 30	Deutsch. med. Wochenschr., 1894, xx.	Paralytic; no bronzing.	Both, L. fist; R. hen egg.	Brain, kidney, peritoneum, mediastinum, pericardium, pancreas.	Short, small, spindle-cell sarcoma.
26	Earl and Weaver	M. 3	Journ. Amer. Med. Assoc., Dec., 1894.	Jaundice; emaciation; rapid increase in size of liver, with improvement, followed by relapses; obliteration of gall-duct.	Right.	None.	Mixed-cell sarcoma.
27	Cohn	F. 9 mo	Berl. klin. Wochensch., 1894, p. 266.	Secondary growth in temporal region; mass felt in abdomen.	Left, 13×5×8 c.m.	Skull, kidney, liver, ovary, ribs.	
28	Drozda	M. 68	Jahrb. Wien., k. u. k. Krankenast, 1895, iv. p. 327.	Mass in abdomen.	Left.	Vena cava.	Sarcoma.
29	Lütke-müller	F. 33	Ibid., p 207.	Weakness, vomiting, emaciation; skin gray-yellow with tinge of brown; black spots on gums.	Both, 5 c.m.× 3.5×1.5	Retroperitoneal glands and mesenteric glands.	Lympho-sarcoma.
30	Caillé	… infant.	Archiv. Pediat., Aug., 1895.	Moribund when seen.	Left.	3d cervical vertebra, diffuse growth.	Round-celled sarcoma, cystic.
31	Affleck and Leith	M. 46	Edinb. Hosp. Rep., 1896, vol. iv.	No pigment; no tumor felt.	Right, 5×4×3in.	Liver, left suprarenal, stomach, pleura, ribs, lymphatics.	Mixed or irregular celled.
32	Affleck and Leith	M. 31	Ibid.	……………	Right, with liver 20 lbs. 4 oz.	Liver, kidney.	Small round-cell.
33	Affleck and Leith	F. 50	Ibid.	……………	Left, 5×4×3 inches.	Continuous, with huge retroperitoneal growth 35¼ lbs.	Cystic sarcoma.
3	Pitt	M. 10 mo	Trans. Path. Soc. London, 1897–1898, xlix.	Jaundice; waisting.	Right, hen egg.	May have started in liver.	Small round-cell.
35	Rolleston and Marks	M. 25	Amer. Journ. Med. Sci., Oct., 1898.	Diagnosis: hydatid of liver; no pigment.	Right.	Aortic lymphatic glands, invaded renal vein, liver, and kidney.	Mixed-cell sarcoma.

No.		Sex and age.	Reference.	Clinical course.	Supra-renal; size, etc.	Metastases.	Variety of sarcoma.
36	Rolleston and Marks, shown by Dickinson to Path.Soc. Lond., 1894	M. 57	Amer. Journ. Med. Sci., Oct., 1893.	Hæmaturia and renal tumor for 8 years; resembled Addison's dis.; pigmentation of axillæ, nipples, and body.	Right, with kidney size of man's head.	Pleura and lungs, liver, extending into vena cava, spleen.	Mixed-cell sarcoma.
37	"	F. 38	Ibid.	No jaundice; œdema of legs; inf. vena cava blocked.	Right.	Liver.	Round-cell sarcoma, hemorrh'ge
38	"	F. 55	Ibid.	No jaundice.	....	Bronchial glands.	Large-cell sarcoma.
39	"	M. 8¾	Ibid.	No jaundice; cerebral symptoms.	Left.	Brain.	Sarcoma.
40	" Muir	M. 31	Ibid.	No pigment.	Right.	Invading liver and kidneys.	Small round cystic sarcoma.
41	"	F. 50	Ibid.	No pigment.	Left.	Large retroperitoneal tumor, 36½ lbs.	Cystic sarcoma.
42	Finny	M. 66	Dublin Journ. Med. Sci., Nov. 1899.	Skin darker than normal; left lung dull; no fluid on tapping; urine normal.	Left, fœtal head.	Right supra and lung, size of pullet's egg.	Mixed-cell sarcoma, giant cells.
43	Brüchanow	F. 32	Zeitschrift für Heilkunde, 1899, vol. xx.	Operated on for supposed subphrenic abscess.	Right, 18 cm. in diameter.	None.	Fibromyxosarcoma.
44	"	F. 58	Ibid.	Abdominal tum., explor. puncture.	Left, man's head.	Few on greater curvature of stomach.	Spindle-cell sarcoma.
45	"	M. 68	Ibid.	Ascites.	Right, 5 cm. in diameter.	None.	Angiosarcoma.
46	Dobbertin	F. 14 mo	Beitr. z. path. Anat. u. z. allg. Path., xxviii. p. 60.	Very hairy child.	Left, child's fist.	Mediastinal and mesenteric glands.	Sarcoma (?)

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THE CARBOHYDRATES OF THE URINE IN DIABETES INSIPIDUS.

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(*From the William Pepper Laboratory of Clinical Medicine, Phœbe A. Hearst Foundation.*)

Recently Rosin and v. Alfthan reported their results from the estimation of the unfermentable carbohydrates of the urine in diabetes mellitus. They make the interesting statement that beside the well-known excretion of glucose in pathological quantities there is in this disease a marked increase in the unfermentable carbohydrates. The daily amount of the total urinary carbohydrates under normal circumstances was never, in their experience, notably more than 5 grammes, and averaged roughly about 1.6 grammes. Similar amounts have been found with normal subjects by several other workers. On the other hand, the smallest daily amount of unfermentable carbohydrate alone in fermented diabetic urine was found by Rosin and v. Alfthan to be about 9 grammes, and in some instances they demonstrated as much as 20 grammes. They conclude from these results that diabetes mellitus can no longer be looked upon as a pure "glucose disease," but is rather a disturbance of carbohydrate metabolism in general.

The method used was precipitation of the carbohydrates by benzoyl chloride in the presence of sodium hydrate. The carbohydrates come down after prolonged shaking of the mixture as benzo-esters, and when the method is properly carried out the precipitate can be fairly readily collected on a filter, washed, dried over sulphuric acid, and weighed. Since the method was described by Baumann it has been investigated by Wedenski, v. Fodor, Roos, Lehmann, Salkowski, Baisch, and Lemaire, and it has been shown that the results obtained indicate with a very fair degree of accuracy the amount of carbohydrate in the urine, when this is small, as is the case under normal circumstances. The precipitate seems to be composed very largely of the esters formed from the carbohydrates, and although there is a slight admixture of nitrogenous matter and salts, and perhaps the esters are in small part not the product of carbohydrates, the error is not sufficient to interfere with the use of the method as an index of variations in the carbohydrate excretion.

Several points in the papers by Rosin and v. Alfthan arrest one's attention. In the first place, they note that it is of interest to learn whether the unfermentable carbohydrates are still excreted in large amounts in diabetes mellitus when the glucose excretion has disappeared under the influence of diet. This might prove to be a point of serious importance in prognosis. Further, v. Alfthan states that in one case of diabetes insipidus which he had under observation, but which at the time of his report had not been completely investigated, the carbohydrates seemed to be increased. If an increase could be shown in a considerable percentage of cases of diabetes insipidus it might indicate an interesting relation between this affection and diabetes mellitus. These suggestions led me to make a series of estimations of the esters formed by this method in the urine of a patient in Dr. Stengel's wards at the University Hospital.

The man, who was an intelligent clerk, aged twenty-seven years, was admitted January 7, 1901, with a history of rather sudden onset, in June, 1900, of polyuria and excessive thirst. This had persisted and had been accompanied by decided loss of weight—about thirty pounds. He stated that his physician had examined his urine repeatedly and had told him that he had diabetes, but he had had no notable increase of appetite and no other symptoms that would strongly indicate the existence of diabetes mellitus, and the urine when he came to the hospital contained no sugar and no acetone, or diacetic acid; albumin and casts were likewise absent. The daily amount of urine was, however, above 4000 c.c., and he had excessive thirst. At the time of admission it was readily discovered that the man was in the early stages of typhoid fever, and he went through a typical mild course of this disease. It seemed possible from the history that he gave that he actually had diabetes mellitus and that the glycosuria had disappeared under the influence of the typhoidal infection. It was with the thought in mind that under such circumstances the benzoyl chloride method might prove to have actual diagnostic value that the estimation of the esters was first undertaken, for a persistent excess in their amount may perhaps be present under such conditions, and if present would probably be a valuable indication of the actual existence of diabetes mellitus in the temporary absence of glycosuria. This point is certainly worthy of investigation, as is the amount of esters found by this method in the urine of those persons who are constantly ready subjects of alimentary glycosuria, those who have hereditary predisposition to diabetes mellitus or other metabolic disturbance, or those who for any other reason are suspected of being ready subjects of diabetes mellitus. The further course of the case under discussion has demonstrated that it is not diabetes mellitus, but, as seemed highly probable from the beginning, diabetes insipidus. Sugar has always been absent from the urine, and the man has had no symptoms excepting undue thirst and polyuria, barring those of typhoid fever. The daily urine now averages about 4500 c.c.

The results obtained in estimating the esters may then be considered solely in their relation with diabetes insipidus. I was unable for a number of reasons to carry out the work until the man had practically begun his convalescence from typhoid fever; the diuresis had been a little reduced by this time through limitation of his fluids so far as was compatible with comfort.

The conclusion that may at once be drawn from the figures in the following table is that the carbohydrates were not increased; the figures obtained by control estimations of the esters and by coincident nitrogen estimations for a part of the time (Kjeldahl method) are given for reasons which will be noted later:

Date.	Amount of urine in c.cm.	Esters in gms.	Nitrogen in gms.
February 7	3670	2.752	. . . .
“ 8	3820	6.494 6.229	. . . .
“ 11	3280	2.427 2.099	. . . .
“ 12	3370	2.830 2.897	. . . .
“ 13	3450	2.484 2.691	14.076
“ 14	4050	2.277 2.754	13.923
“ 15	4100	1.517 1.413	12.628
“ 16	2120	1.611 1.484	8.814
“ 18	3400	1.666 1.768	15.803
“ 19	1800	1.512 1.368	11.551
“ 20	1840	1.325 1.288	9.991

The figures of February 8th are, to be sure, somewhat abnormally high, but they are so wholly at variance with all the other results in this case that I am inclined to think that there was an error in technique. The close correspondence of the control results speaks against this (the two estimations were carried out separately from the beginning), but even though the figures be correct the result is such an isolated one that it deserves no special comment, and all the other figures are wholly within the normal range. So far, then, as this case goes the results speak against the probability of any marked increase in the urinary carbohydrates in diabetes insipidus. One would certainly be inclined to anticipate this from the beginning, as no other similar relation between this disease and diabetes mellitus has been demonstrated. I should not be surprised, however, were a rather high excretion of urinary carbohydrates shown to be present in many cases of diabetes insipidus as a result of the excessive diuresis alone, not as an indication of disturbed carbohydrate metabolism. An increase of the urinary carbohydrates in this disease, unless very marked, could scarcely be looked upon as evidence of any primary disturbance of the metabolism of carbohydrates, for it is well known that flushing the system with large quantities of water will cause a marked increase of the nitrogen output, and I have shown that this persists over a considerable period, and perhaps constantly so long as the excessive amounts of water are taken; a positive nitrogen balance may even be converted into a nitrogen loss in this way. Similar results were obtained by Ter Gregorianz and Karchagin in normal subjects in nitrogen equilibrium, and by Matzkevich and Grusdiev in subjects of typhoid fever who showed a negative nitrogen balance. It is wholly probable, then, that the constant flushing in diabetes insipidus may carry off an abnormally large amount of carbohydrates in the urine, and that a portion of the increase in diabetes mellitus which was observed by Rosin and v. Alfthan may be due to the same cause, though this alone could not produce the very marked change seen in the latter affection. Another fact which would lead one to expect an increase with the free diuresis of diabetes insipidus is that actual glycosuria may be produced by some diuretics which act directly upon the kidney. That increase or decrease in the diuresis does cause an increase or reduction in the urinary carbohydrates is, I think, shown fairly definitely in the table given above. From February 15th to February 20th, inclusive, the man's fluids were reduced to as low a point as was possible without causing serious distress. The excretion of urine remained high on the 15th, though he certainly got only about 3000 c.c. of fluid in both food and drink during that day. On the 16th, 17th, 19th, and 20th the excretion was far lower than at any other period of observation. (The amount of urine on the 17th was 1780 c.c., but the esters were not estimated.) The average figures for the esters up to February 14th (excluding the result on February 8th, which is very probably incorrect) is 2.598 grammes; for the period from February 15th to February 20th, inclusive, 1.499 grammes. Hence the restriction of fluids reduced the esters to 58 per cent. of their previous amount. If the two periods be made according to the drop in the excretion of urine it is interesting to note that the average of esters for the period from February 7th to February 15th, inclusive, is 2.410 grammes, while for that from February 16th to February 20th, inclusive, is 1.502 grammes, while the average amount of urine in the same periods is 3650 c.c. and 2290 c.c. respectively. The average amount of esters in the second period is, then, 62 per cent. of the average in the first period, while the average amount of urine in the second period is 63 per cent. of that in the first period. This correspondence between the diuresis and the amount of esters, while its exactness is probably largely accidental, is too close to allow one to overlook the fact that the two bear a decided relation to each other. Diet could have played no part in this, as absolutely the only change made in the man's regimen was in the amount of water given him. Throughout the whole series of estimations he was given exactly the same food in constant quantities; the food consisted of milk, eggs, butter, bread, and sugar. The amount of carbohydrates in the urine is, therefore, evidently influenced to a very decided degree by the amount of urine passed and very probably, as suggested by Rosin and v. Alfthan, by the diet also. It is quite possible that excessive diuresis is sufficient to explain the result obtained by v. Alfthan in his case of diabetes insipidus, and it would certainly be necessary to demonstrate a very marked increase in order to show by this method even a probable relation between diabetes mellitus and diabetes insipidus so far as carbohydrate metabolism is concerned. If further investigation should show a moderate increase of esters in diabetes insipidus I should be very strongly inclined to attribute this increase wholly to the abnormal diuresis. The man whose case I report did not show any increase at the time of the investigation, but it would not surprise me if another series of estimations undertaken in the same case after six months or a year had passed demonstrated larger quantities of carbohydrates than those reported here, for the man was, as stated, convalescing from typhoid fever when these estimations were made. A marked tendency toward the laying on of tissue after severe acute diseases is demonstrated both by clinical observation and by exact determinations of the intake and outgo in such subjects. This man was increasing in weight and was evidently retaining nitrogen, as his food contained about 15 grammes of nitrogen while his excretion in the urine was notably more than 14 grammes in only one instance. It seems to me that he was very probably excreting less carbohydrates also than would be the case under ordinary circumstances. At any rate, this possibility is of sufficient interest to deserve investigation in other instances.

The nitrogen was estimated for a number of days coincidently with the esters for two reasons: To see whether there was the same relation between the amount of fluids taken and the nitrogen excretion that I have previously referred to; and to see whether there was any relation between the nitrogen excretion and the excretion of carbohydrates. The latter point was chiefly of interest because v. Alfthan stated that he thought that the unfermentable carbohydrates may be looked upon as derived from body protein or from glycogen—*i. e.*, that they are produced in the body. If they are derived from body protein their excretion should show some relation to the nitrogen excretion if the nitrogen intake is kept constant, as was practically the case with this man. In regard to the latter point the ratio of esters to urinary nitrogen was as follows: February 13th, 1 to 5.44; February 14th, 1 to 5.53; February 15th, 1 to 8.5; February 16th, 1 to 5.69; February 18th, 1 to 9.2; February 19th, 1 to 8.02; February 20th, 1 to 7.65. There was a general tendency for the nitrogen and the esters to rise and fall together, as most of the urinary solids tend to do in a general way. There was not the slightest tendency, however, toward the maintenance of any fixed ratio in the excretion of the two, and so far as such an observation goes it points against the formation of the urinary carbohydrates in this case from body protein. So complex a question cannot be settled in this off-hand manner, however, and this point in the figures is not worthy of much insistence. The question of the origin of the carbohydrates will be touched upon again at the end of this paper. The nitrogen excretion shows, in general average, the same rise and fall with increase or decrease of intake of fluids that I have previously described, and I think that it is quite thoroughly established by the observations to which I have referred and by my own earlier results that excessive water ingestion increases protein metabolism—a fact which is, as I have previously insisted, of much importance in explaining the clinical results of immoderate use of fluids.

There are one or two points concerning the benzoyl-chloride method that may be worthy of mention. In the first place, it is absolutely essential to have a good preparation of benzoyl chloride—a fact which is not sufficiently insisted upon by those who have previously discussed the method. Some of the difficulties in the use of the method described by several authors were not improbably due to the use of impure benzoyl chloride. I tried in all ways that I could devise to obtain a satisfactory precipitate with what was thought to be a perfectly satisfactory preparation, but had no success in about two weeks' work. I then secured some benzoyl chloride from another source, and afterward met with absolutely no difficulty in carrying out the method. The first specimen was undoubtedly faulty, though it was not evident in what way, and I made no serious attempt to learn what was wrong. In carrying out the method one should be careful to shake the mixture gently at first in order to avoid producing an emulsion. If shaken gently for ten minutes, or thereabouts, and then more vigorously for about twenty or twenty-five minutes, the esters precipitate extremely well and can be washed readily. I found it unnecessary to shake the mixture for "at least one hour," as recommended by a number of writers. Finally, Salkowski recommended that the mixture be shaken for a half-hour and then stood aside overnight before filtering. This is, I think, unsatisfactory. I have had good flocculent precipitates become sticky and impossible of filtration after such a procedure. The esters tend to become sticky after standing even when they have been washed and placed in a closed vessel over sulphuric acid.

The figures for control estimations were introduced into the table merely to show that absolutely exact results are not obtained by the method. It has been the general experience that control estimations are likely to show variations in results as large as 10 per cent. or more. My results show this in most instances. Two estimations were made every day after the first, the whole process being carried out separately in each case, even in precipitating the phosphates before adding the benzoyl chloride. Exactly the same amount of urine, of benzoyl chloride, and of sodium hydrate was used in each estimation, the mixtures were shaken for the same length of time, cooled in the same manner, filtered coincidently, and each was washed just to the point where the filtrate became neutral, yet the decided variations shown were not avoided. These variations are, however, not sufficient to make the method of questionable value when used only as an index and when, as in the work herein reported, small variations have no influence upon the conclusions reached.

v. Alfthan states that his results in estimating the esters in a normal subject throughout a series of twelve days showed figures varying from 1.5 grammes to 5.1 grammes. My patient showed much more constant excretion. When taking large quantities of fluid the esters varied only between 2.099 grammes and 2.897 grammes, exclusive of the wholly erratic result on February 8th. The amount fell when the fluid was reduced, but there was only slight subsequent variation, the figures ranging only between 1.768 and 1.288. Since this man was on constant diet, and there is no statement that such was the case with v. Alfthan's (normal) subject, who showed such marked variations, it seems to me extremely probable that the amount of carbohydrates in the normal urine depends largely upon the diet, and that these carbohydrates are in large part at least derived from the food rather than formed in the body. I would say again, however, that this question is still widely open.

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CARCINOMATOUS DEGENERATION OF A PAPILLOMA OF THE CONJUNCTIVA WITH INFILTRATION OF THE EYELIDS.*

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ILLUSTRATED.

In the last number of Graefe's Archiv. für Ophthalmologie (Vol. LI, p. 127), O. Koptezky von Rechtperg reported a case of papilloma of the conjunctiva which had undergone carcinomatous degeneration, destroying the conjunctiva and penetrating into the interior of the eyeball. He was unable to find any similar case in literature, in which a histological examination had been made. The following case which is interesting from the involvement of the eyelids at the outer canthus, was seen at the Will's Hospital clinic. The history is as follows;

John Maher, Aet. 65, came to the clinic with a large granular mass covering the greater part of the outer half of the left eyeball, stretching well back into the retro-tarsal folds at the outer canthus and spreading over the outer half of the cornea. It presented a papillomatous appearance but was very friable, tearing readily when grasped with the forceps and bleeding freely. The outer two-fifths of both upper and lower lids and the external canthus were much thickened by infiltration and hard. The growth had been removed from the ball by another surgeon several months before, but had quickly returned and spread with great rapidity, assuming the proportions described. The man was admitted to the hospital, and a portion of the tumor removed from the ball and submitted to Dr. E. A. Shumway for histologic examination, who reported it of carcinomatous nature. The removal of the eyeball and the portion of the lids involved in the disease was therefore advised and the operation at once performed. After enucleation there appeared to be no thickening of the deeper orbital tissues so that exenteration of the orbit did not seem advisable. The lids at the external canthus were then seized between the thumb and finger and all the thickened portion excised with a pair of curved scissors. The mucous and skin surfaces were united with interrupted sutures. The recovery was uneventful and the man was permitted to return to his home in the interior of the state with the request that he report his condition by postal card every month. This he has done faithfully and reports that he is perfectly well. The eyeball and the portion of the lids excised were placed in Dr. Shumway's

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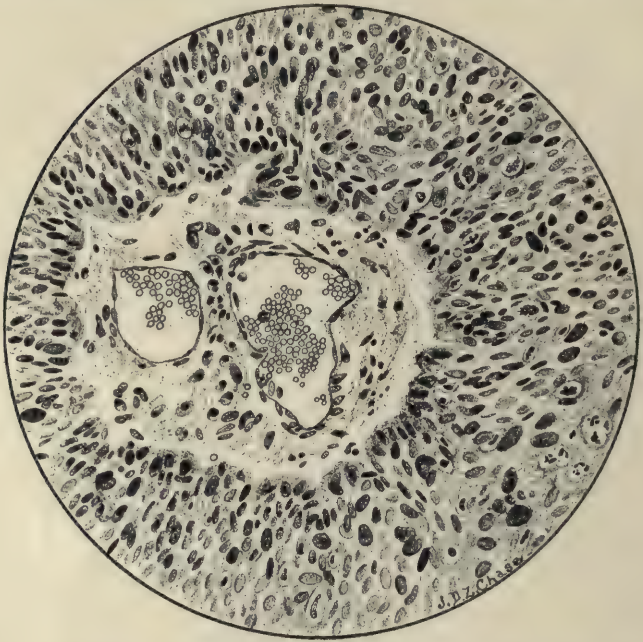

Fig. 1. Section of Growth from Conjunctiva Showing Cross Section of a Papilla, Unusual Size of Cell Nuclei, and Number of Karyokinetic Figures.

hands for laboratory study. His report follows together with a bibliography of reported cases:

PATHOLOGICAL REPORT.*

The pieces of tissue from the conjunctival growth, and from the infiltrated eyelids were embedded either in celloidin or paraffine; the eyeball was embedded in celloidin, after careful hardening. Most of the sections were stained in haematoxylin-eosin. Those of the growth and of the eyelids approximated 10 micromillimeters in thickness. Sections of the eyeball were also stained for micro-organisms, by the Gram-Weigert method.

The specimen removed from the conjunctiva measures 10×8×6 mm. It shows the typical arrangement of conjunctival papilloma which has been thoroughly described, in recent years, by Elschnig,[2] S. Fuchs,[3] Wagenmann,[4] etc. The central vessels of the branching connective tissue axes, are usually two in number, and possess very thin walls; they are distended with blood, and surrounded by a loose meshed, fibrillar connective tissue, which contains but few cells; here and there are collections of infiltrating leucocytes. In direct application to the connective tissue axes, are the epithelial cells which form the thick mantles. These cells (see Fig. 1) are worthy of especial attention on account of their size and arrangement. The innermost are cylindrical in shape, and are arranged with their long axes perpendicular to the axis of the vessel. There is but little evidence of a basement membrane, and, even in this position, it is almost impossible to distinguish the outlines of the cells, the nuclei seeming to be in a homogeneous ground substance. Further toward the periphery, where the cells are more irregularly arranged, this becomes still more marked; the nuclei stain deeply and are very large, measuring in some instances 29 micromillimeters in the long diameters (four times the size of a red blood cell), while nuclei which have a diameter of 19 micromillimeters are by no means uncommon. There are also an unusually large number of karyokinetic figures in all stages of development, and, in contrast to the ordinary forms of this tumor, there is very little flattening of the surface cells, no loss in the staining power of the nuclei nor the slightest indication of a horny change. Scattered through the cells are occasional leucocytes; these are more numerous on the surface, and are mixed with blood cells, especially between the lobules composing the tumor.

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*June 25th, 1901. Report from patient two years after operation, no return of disease.

The growth on the cornea was separated from the conjunctival portion, at the time of operation, so that the direct connection between them cannot be shown in the sections of the eyeball. Bowman's membrane is destroyed throughout the entire surface of the cornea, as far as the sections reach; the lamellae of the substantia propria are irregular in arrangement, and show a few newly formed vessels, and some round cells. The tumor occupies the temporal half of the cornea and is composed of cells showing the same characteristics as those of the conjunctival portion, except that the nuclei are not so large, there are fewer karyokinetic figures, and the cell outlines can be more readily distinguished. The mass is about 1.5

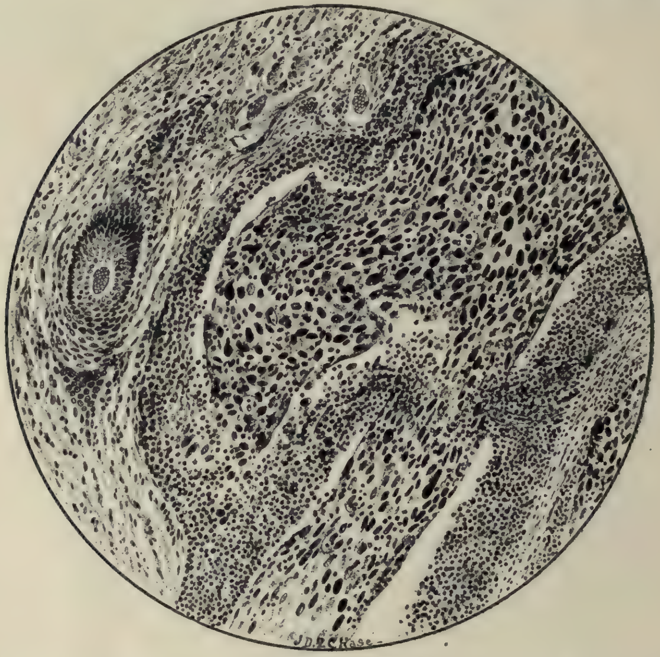

Fig. 2. Section from Infiltrated Eyelids. Solid Process of Epithelial Cells. Surrounding Tissue Infiltrated with Round Cells. Cross Section of Hair Bulb to the Left.

mm. high, and is separated from the corneal lamellae by masses of round cells, so that there is no infiltration of the cornea itself by the epithelial cells. The deeper structures of the eyeball shows marked hyperaemia, and the posterior pigment layer of the iris is agglutinated to the anterior capsule of the lens, but, aside from these changes, the eyeball is normal.

On examining the sections of the eyelids, at the outer canthus, they are seen to be infiltrated with precisely the same cells as those of the tumor on the conjunctiva and cornea. The nuclei are large, oval, darkly staining and the cell outlines are rather indistinct. The type is the same, but their arrangement has been changed. Instead of central axes of connective tissues covered with epithelial mantles, we find solid processes of tumor cells, contained in definite alveoli, extending through the connective tissue of the eyelids, and accompanied by dense collections of round cells. (See Fig. 2). In other words, the tumor has changed in type from that of papilloma to that of carcinoma, and differs from the ordinary skin carcinoma of this region only in the type of the cells, which is that of the conjunctival epithelium, instead of skin epithelium, in the absence of whorls of cells—so-called "pearly bodies," and of any attempt at a horny change.

This case like that of v. Rechtperg's, in which the cornea was destroyed by the infiltrating mass, is one of papilloma, originally benign, but, which, on account of its rapidity of growth, has become essentially malignant. So far as the literature at our command has sufficed, a similar case of secondary infiltration of the eyelids by a conjunctival papilloma has not been found. v. Rechtperg gives two cases besides his own, in which malignancy was shown. The first, reported by Horner,[5] was that of a man 62 years old, in which there was recurrence after removal of a large papilloma, with subsequent destruction of the cornea and penetration of the globe. In the second, by La Grange and Mazet,[6] there was a similar recurrence and involvement of the cornea. In neither of these cases had an histologic examination been made, so that v. Rechtperg's case was the only one published where malignancy was proved by the microscope. The majority of the writers on the subject: S. Fuchs,[3] Grünert,[7] Caspar,[8] Weeks[9] and others have denied that papillomata of the conjunctiva ever become malignant, in the sense of destroying surrounding tissues, although among general pathologists (Hirschfeld,[10] Billroth,[11] Ziegler[12]) the opinion has long been held that papillomata of the mucous membranes, especially those of the bladder, may, at times undergo carcinomatous degeneration. v. Rechtperg thinks that this has not been observed on the conjuctiva, because the growths have always been removed, as soon as possible, on account of their tendency to recur. His case, however, with those of Horner, and La Grange and Mazet, and the one reported by us, show that occasionally it may occur, especially when the age of the patient is advanced. This should, therefore, be an additional reason for their early and radical removal, together with all affected tissue, even of the eyeball itself, if the growth is distinctly adherent to it.

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CONTENTS.

1 A Case of Cervical and Bulbar Tabes, with Necropsy. Microscopical Study and Comments . . . . William G. Spiller, M.D.

2 A Case of Complete Absence of the Visual System in an Adult. —William G. Spiller, M.D.

The Sensory Segmental Area of the Umbilicus . . . . William G. Spiller, M.D.

A Case of Primary Degeneration of the Pyramidal Tracts. —William G. Spiller, M D.

5 Two Cases of Partial Internal Hydrocephalus from Closure of the Interventricular Passages . . . . William G. Spiller, M.D.

6 Case of External Spinal Pachymeningitis, Implicating the Entire Ventral Surface of the Spinal Dura. —Charles K. Mills, M D., and William G. Spiller, M.D.

7 The Division of the Sensory Root of the Trigeminus for the Relief of Tic Douloureux: An Experimental, Pathological, and Clinical Study, with a Preliminary Report of One Surgically Successful Case. —William G. Spiller, M.D., and Charles H. Frazier, M.D.

8 A Further Report upon the Treatment of Tic Douloureux by Division of the Sensory Root of the Gasserian Ganglion. —Charles H. Frazier, M.D., and William G. Spiller, M.D.

9 Acute Alcoholic Multiple Neuritis with Peculiar Changes in the Gasserion Ganglia. —Charles W. Burr, M.D., and Daniel J. McCarthy, M.D.

10 Cerebral Lesions in Experimental Lead Intoxication . . . . D. J. McCarthy, M.D.

11 Melanosis of the Cerebro-Spinal Meninges. —D. J. McCarthy, M.D., and Mazyck P. Ravenel, M.D,

12 The Estimation of the Urinary Sulphates and of the Fecal Fat in the Diagnosis of Pancreatic Disease . . . . D. L. Edsall, M.D.

13 A Contribution Concerning Creatinin Excretion . . . . David L. Edsall, M.D.

Concerning the Benzoyl Esters of the Urine in Diabetes Mellitus, and the Clinical Significance of an Excess of Glycuronic Acid . . . . D. L. Edsall, M.D.

15 Specific Gravity of the Urine and Nitrogen Elimination in Pregnancy. —Caspar W. Miller, M.D.

CONTENTS.

16 A Study of the Post-Operative Changes in the Blood.
—CHARLES H. FRAZIER, M.D., and THOMAS B. HOLLOWAY, M.D.

Myositis Fibrosa . . . . M. H. BIGGS, M.D.

18 Further Studies of Granular Degeneration of the Erythrocyte.
—ALFRED STENGEL, M.D., C. Y. WHITE, M.D., and WILLIAM PEPPER, M.D.

19 Sarcoma of the Large Intestine.
—JOHN H. JOPSON, M.D., and COURTLAND Y. WHITE, M.D.

20 Carcinoma of the Eyelids, with Secondary Involvement of the Eyeball; Removal of the Growth by Extensive Plastic Operations; Recurrence.
—WM. CAMPBELL POSEY, M.D., and EDWARD A. SHUMWAY, M.D.

21 Papilloma of the Caruncle, with Report of a Case.
—WM. CAMPBELL POSEY, M.D., and EDWARD A. SHUMWAY, M.D.

The Surgical Treatment of Sterility due to Obstruction at the Epididymis. Together with a Study of the Morphology of Human Spermatozoa.
—EDWARD MARTIN, M.D., J. BERTON CARNETT, M.D., J. VALENTINE LEVI, M.D., M. E. PENNINGTON, Ph.D.

Extracted from The American Journal of the Medical Sciences, August, 1901.

A CASE OF CERVICAL AND BULBAR TABES, WITH NECROPSY.[1]

MICROSCOPICAL STUDY AND COMMENTS.

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OF PHILADELPHIA.

(*From the William Pepper Clinical Laboratory, Phebe A. Hearst Foundation.*)

No distinct degeneration is found in the posterior columns in the mid-lumbar region. The nerve fibres along the posterior septum are not quite so numerous as elsewhere in the posterior columns, but no positive degeneration is found even here. Some of the bundles in the extramedullary portion of the posterior roots show a slight degeneration, but the medullated nerve fibres passing into the posterior horns are numerous. It is doubtful whether the anterior roots could be regarded as at all degenerated. When the lumbar posterior roots are collected and cut separately from the cord so that a large number may be obtained in transverse sections, very little degeneration of these roots is seen. The nerve cell bodies in the anterior horns are numerous and are apparently normal.

In the mid-thoracic region there is no pronounced degeneration of the postero-median columns. The nerve fibres possibly are not quite so numerous along the posterior septum as in a normal cord, but the diminution in the number of the fibres, if it exists, is very slight. When a large number of posterior roots are cut separately from the cord they are found to be much degenerated, and some of the bundles contain no medullary nerve fibres at all, and others very few such fibres. (See Fig. 1.) Even macroscopically the atrophy of the posterior roots of this region was very perceptible when the spinal cord was examined. The bloodvessels within the degenerated posterior roots have much thickened walls and are of a glassy, homogeneous appearance when stained with ammonium carmine. A slight area of sclerosis is seen on the median side of each posterior horn in the area of the root entrance zone.

In the lowest cervical region, at what is doubtless the eighth segment, the posterior columns appear to be normal except in a narrow band within the column of Burdach along each postero-lateral septum and in the right root entrance zone. The left root entrance zone appears to be almost normal. This narrow band of slight degeneration along each postero-lateral septum is the result of partial degeneration of posterior roots in the upper thoracic region. The root entrance zone on the right side in the eighth cervical segment is much degenerated, as is also a portion of the extramedullary posterior root of this segment. At the cervico-thoracic junction—*i. e.*, a little lower—the posterior roots in their extramedullary portions are intensely degenerated. At the eighth cervical segment the posterior root on the left side is almost

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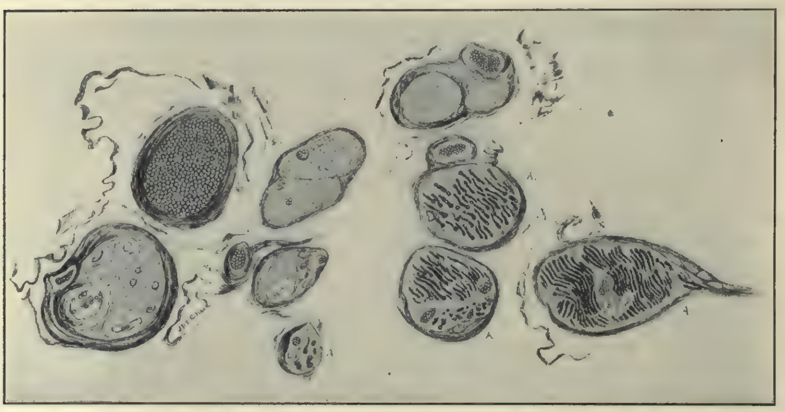
[1] The clinical report of this case by Dr. S. Solis Cohen is to be found in the AMERICAN JOURNAL OF THE MEDICAL SCIENCES, August, 1901.

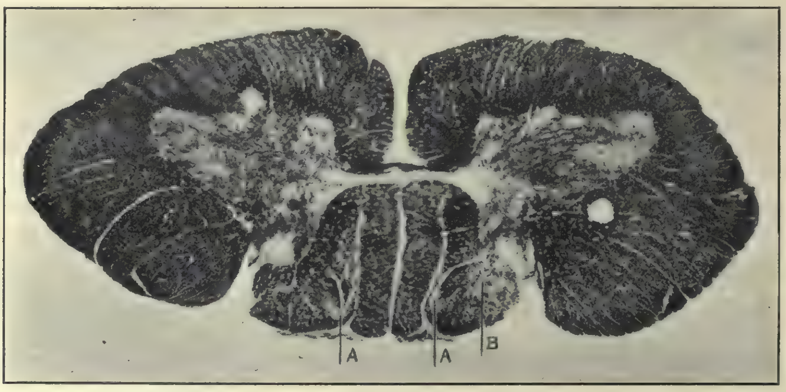
normal. On the right side the posterior roots in the lower cervical segments (see Fig. 2) are partially degenerated, and fewer medullary fibres are found entering the right posterior horn than the left ; at the mid-cervical region no degeneration even of the right posterior roots is seen. A small but distinct area of degeneration in the lower cervical region above the eighth segment is found in each column of Burdach near the periphery of the cord and adjoining the postero-lateral septum, and is in the same position as in the eighth cervical segment. It is the result of degeneration of upper thoracic posterior roots. The degeneration of the posterior roots in the cervical region is almost confined to the right

FIG. 1.



Posterior roots of the mid-thoracic region, cut transversely. The bundles A, A, A, A are much degenerated. The nerve fibres have entirely disappeared in the other bundles.

FIG. 2.

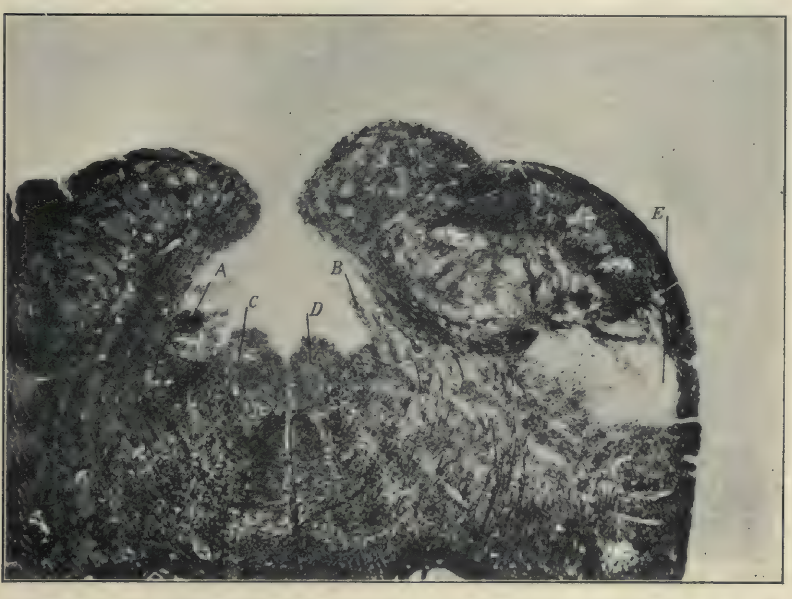


Photograph of a transverse section of the spinal cord from the lower cervical region. A, A. Narrow band of degeneration along each postero-lateral septum, the result of partial degeneration of posterior roots in the upper thoracic region. B. Degenerated root entrance zone on the right side. The corresponding zone on the left side is not degenerated.

side and the lower cervical levels. No recent degeneration is detected by the Marchi method in sections from the lower cervical region, and the process was evidently not acute. The anterior roots are normal. No distinct round-cell infiltration of the pia of the cord is present. The nerve cell bodies in the anterior horns are numerous and highly pigmented, which is not extraordinary in consideration of the age of the patient.

Sections from the lower part of the medulla oblongata show no degeneration with Marchi's stain. The nucleus of the left twelfth nerve in its inferior portion is much smaller than the corresponding portion of the right twelfth nucleus (see Fig. 3), and contains fewer nerve cell bodies and fewer medullated nerve fibres. The intramedullary nerve fibres of the left twelfth nerve are not so numerous as those of the right in the inferior portion of the medulla oblongata, but at higher levels a distinct difference between the two nuclei and the intramedullary fibres of the twelfth nerves cannot be observed, and there is no distinct degeneration of these parts. The extramedullary portion of each twelfth nerve is normal.

FIG. 3.



Photograph of a section from the lower part of the medulla oblongata. The nucleus of the left twelfth nerve (D) is much smaller than that of the right twelfth nerve (C) at this level. The descending root of the ninth and tenth nerves on the left side (B) is degenerated, while that on the right side (A) is normal. The spinal root of the fifth nerve (E) is degenerated on each side, but not so completely as the photograph represents, as under the microscope it contains a few nerve fibres.

The posterior nucleus of the tenth nerve is normal on each side. It is difficult to determine a moderate degeneration of the nucleus ambiguus, but on neither side is this nucleus distinctly degenerated. Some of the nerve cell bodies in this nucleus on each side are much pigmented. The fasciculus solitarius on the left side is greatly degenerated, but on the right side this fasciculus is normal. (See Fig. 3.)

Along the floor of the fourth ventricle are proliferations of neuroglia forming irregular projections into the ventricle.

The lemniscus is normal.

There is some slight perivascular round-cell infiltration in the pia and within the medulla oblongata, but this is not important.

The seventh nucleus and intramedullary fibres of the seventh nerve on each side are normal. The extramedullary portion of the left seventh nerve is probably slightly degenerated, but sections from a corresponding portion of the right seventh nerve appear to be normal.

The nucleus and intramedullary fibres of each sixth nerve appear to be normal. The right sixth nerve in its extramedullary portion is partially degenerated, while the left sixth nerve in the corresponding portion is apparently normal.

In the sections examined the fifth motor and sensory nuclei are present only on one side, and these nuclei are normal. A transverse section through the extramedullary portion of the left fifth nerve near the pons shows considerable degeneration of the nerve roots. The spinal root of the fifth nerve on each side is much degenerated, and possibly the ventral portion is a little more degenerated than the dorsal in the inferior part of the medulla oblongata.

The right cerebral peduncle is considerably smaller than the left.

Sections through the oculomotor nuclei contain many nerve cell bodies in each lateral nucleus and in the median nucleus, but the nerve cell bodies in the left lateral nucleus are distinctly fewer than in the right, and cell bodies in all parts of the oculomotor nuclei are atrophied, deeply pigmented, and have peripherally situated nuclei. The contrast is striking in comparison with nerve cell bodies of an oculomotor nucleus believed to be normal.

The giant-cells of the left paracentral lobule are normal, but in some portions of the cortex from this part the capillaries are very numerous.

The right optic nerve appears to be normal, but the left is partly degenerated.

The important findings in this case are: Degeneration of the posterior roots of the spinal cord, hardly perceptible in the lumbar and lower thoracic regions, very distinct in the middle and upper thoracic and on the right side in the lower cervical region but absent in the middle and upper cervical regions. No distinct degeneration of the columns of Goll, and very slight and limited degeneration of the columns of Burdach in the upper thoracic and cervical region; atrophy of the inferior part of the left twelfth nucleus; integrity of the extramedullary roots of the twelfth nerves; intense degeneration of the left descending root of the ninth and tenth nerves, possibly a slight degeneration of the extramedullary portion of the left seventh nerve near its exit from the medulla oblongata; partial degeneration of the extramedullary portion of the right sixth nerve; intense degeneration of the spinal root of each fifth nerve, with partial degeneration of the extramedullary portion of at least one fifth nerve; atrophy and changes in the nuclei of the oculomotor nerves, resembling those occurring when the axones are diseased.

These lesions justify the diagnosis of an atypical form of tabes, and the data of importance in the clinical history are: The acquisition of syphilis some years before the appearance of symptoms of nervous disease ; attacks of nocturnal incontinence of urine beginning in 1872 ; a peculiar form of ptosis of the right eye beginning in 1878 or 1879—*i. e.*, a drooping of the right upper lid, which might have been the result of partial paralysis of the levator palpebræ superioris or of loss of the muscular sense in the lid. The lid could be raised voluntarily, but was more comfortable closed—" springing pupils" dating from 1878 or 1879 ; it is stated that the contraction and dilatation of the pupil in each eye varied from time to time; some weakness of the facial muscles which may have been the result of loss of muscular sense in the face, as it seems that co-ordinated movements, such as whistling, were most affected; difficulty of mastication and of deglutition; atrophy of the tongue, noticed at first on the left side; disturbance of sensation, especially for temperature and pain, and especially on the right side of the face, which seems to suggest that the right-sided ptosis may have been of centripetal rather than centrifugal origin—*i. e.*, from implication of the muscular sense; occasionally griping pains in the abdomen, not due to indiscretion in food or ordinary causes; and neuralgic pains in the lower limbs, these seeming to be the lancinating pains of tabes; a " suspicious grayness" of the optic disk, inequality of the pupils, loss of reaction of the irides to light, loss of power of accommodation, weakness of the right external rectus muscle, failure of vision—all observed by Dr. Jackson in 1888—loss of sexual power.

In addition to these symptoms atrophy of the upper limbs and pain in the ulnar distribution of the right hand developed, the latter explicable by the degeneration of the posterior roots in the lower cervical and upper thoracic regions on the right side.

It is remarkable that this man had no inco-ordination in the movements of the upper limbs, and that he had not is very evident from a specimen of his handwriting. Dr. Cohen says he had no distinct inco-ordination, and was able to write well and clearly and to do work in his carpenter shop up to within a few weeks of his death. The absence of ataxia is explained by the fact that in the cervical region only the lowest posterior roots were degenerated, more especially those on the right side, and even here these roots contained many normal fibres. The degeneration of the posterior roots in the upper thoracic region explains the severe pains extending into the abdomen.

Dr. Cohen, in his paper published eleven years before the death of the patient in 1900, remarked that he believed an irregularly diffuse and slowly progressive degenerative lesion existed, affecting principally the medulla oblongata. The microscopical examination of the tissues shows that this opinion was correct. The slowness in the development of this atypical form of tabes was most extraordinary, for even after the disease had existed many years, presumably at least since 1878 or 1879, the degeneration of the posterior roots was almost confined to the upper thoracic and right lower cervical regions, and was not complete in these portions. The degeneration of the posterior columns was slight, and was partially masked by the presence of normal fibres from lower levels of the spinal cord. The sections are totally unlike those of the ordinary form of tabes, as the columns of Goll are nearly or fully intact.

It is exceedingly important to note that when this case was reported by Dr. Cohen, in 1889, and at a time when the symptoms of the disease were very pronounced, the knee-jerks were well preserved. The explanation is found in the almost complete integrity of the posterior roots of the lumbar region. The knee-jerks in cervical tabes have usually been absent.

The mentality in Dr. Cohen's patient does not seem to have been fully normal, because it is stated that there was some disposition to repetition of old stories and a forgetfulness of details. Marie[1] has said that in bulbar tabes mental disturbance is not uncommon, and, indeed, it is not very uncommon in the ordinary lumbar form of tabes.

In 1889 co-ordination was said to be perfect, the patient could execute complicated movements with precision, could stand with the eyes closed, and could balance himself on one foot. As Dr. C. K. Mills pointed out at that time, the symptoms were those of bulbar paralysis, but yet the case was unlike one of bulbar paralysis on account of the marked changes in the pain and temperature senses below the neck as well as above it; the involvement of the bladder, bowels, and sexual organs; the general wasting, and the attacks of pain with vasomotor and trophic changes. It is not astonishing that syringomyelia was thought of. The dissociation of sensation, impairment of pain and temperature senses with greater integrity of tactile sense, was like the disturbance of sensation in syringomyelia, and in 1889 syringomyelia was not so well understood as in 1901. We now know that dissociation of sensation may occur in tabes.

The condition known among the Germans as "springing pupils" ("springende Pupillen"), or "springing mydriasis," deserves attention. Koenig[2] says it is of rare occurrence, and comparatively little has been written on the subject. It has been observed in paretic dementia and tabes, and regarded as a bad omen, but is not necessarily so. It has preceded most of the other signs of paretic dementia five or twelve years (Mendel, Hirschberg). It consists of transitory mydriasis affecting first one eye and then the other, and while it may be found in persons without organic nervous diseases, it should at least make the diagnostician guarded in his statements regarding prognosis. Riegel[1] also believes that it is not necessarily a bad sign. In Dr. Cohen's case the sign was very prominent, and was observed among the first manifestations of disease.

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[1] Traité de Méd., vol. vi. p. 415.

[2] Deutsche Zeitschrift für Nervenheilkunde, vol. xv., Nos. 1 and 2, p. 122.

I have not found any reported cases of cervical tabes in which the alteration was in the early stages of the disease, as in this case I have studied, and which so far as the spinal cord was concerned was not only a case of tabes superior, but also one of tabes insipiens. The nerve fibres were not all diseased even in those posterior roots that were most altered, and consequently degeneration of the columns of Burdach is not very intense, because normal fibres in these columns are so intimately mingled with the degenerated fibres that sclerosis has not become prominent, and yet the degeneration was not recent, as no evidence of recent alteration was obtained by Marchi's method. For some mysterious reason the disease of the posterior root fibres progressed very slowly, and seems to have been almost arrested for years, as we may judge from the slow progress of the clinical symptoms and the slow death of the posterior root fibres.

A. Stcherbak[2] is correct when he says we must assume that in the early stages of tabes all the root fibres in the various segments of the cord are not equally affected. The case I have examined permits more than an assumption, and shows that there is a very incomplete degeneration of any one posterior root. It is because of this fact that there are many variations of the clinical phenomena; possibly the fibres conducting the sensory impressions from the skin may be first affected or those from deeper structures, so that in the early stages of tabes there may be disturbance of the cutaneous sensation alone, or loss of the deep sensation without disturbance of cutaneous sensation, or ataxia without disturbance of sensation.

The cases of cervical tabes with necropsy, so far as I have been able to collect them from the literature, are those of Leyden, Dejerine, Martius, Eichhorst, Marinesco, Redlich, and probably those of Mayer and Vucetie. The name of tabes cervicalis seems to have been first employed by the elder Remak for that form of tabes in which the upper limbs are chiefly implicated. It is a very rare type of the disease, and in 106 cases of tabes studied at the Bicêtre, Dejerine[3] observed it only once. It is known also as tabes superior, and on account of its resemblance clinically to syringomyelia Marie[4] warns us to be careful in the differential diagnosis. Very few cases have been reported in the literature, and if we include only those with necropsy the number is exceedingly small. The only cases of tabes cervicalis referred to by Leyden and Goldscheider,[1] in their recent work in the Nothnagel system of monographs, are those of Leyden, Martius, Dejerine, and Redlich. Redlich,[2] in his monograph on tabes, in which we should expect to find the literature fully given, refers to the cases of Leyden, Martius, Eichhorst, Dejerine, Vucetie, Marie, Mayer, and Marinesco. In an earlier paper on tabes, Redlich[3] described a case of cervical tabes, and in his monograph already referred to he describes another. It is desirable to collect these cases of cervical tabes so far as possible, and to compare the symptomatology. In the few that are reported with necropsy the degeneration of the posterior roots does not seem to have been confined to the cervical region, so that in a strict sense tabes cervicalis is a misnomer, but it has been long in use and the predominance of the symptoms is the result of cervical implication, and it is therefore likely that the term will not be abandoned.

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[1] Deutsche Zeitschrift für Nervenheilkunde, vol. xvii., Nos. 1 and 2, p. 169.

[2] Neurologisches Centralblatt, 1900, No. 23.

[3] Sémiologie du Système Nerveux. Traité de Path. Gén., vol. v. p, 650.

[4] Vorlesungen über die Krankheiten des Rückenmarkes, translated from the French, p. 325.

In 1876, in his "Klinik der Rückenmarkskrankheiten," Leyden[4] said: "In rare cases the disease begins in the upper limbs; the pains and sensory disturbances are felt here first, and remain most severe here. The lower limbs during the entire course of the disease are not much affected. A case of this kind was described by Gull, and I have recently observed a similar one. The recognition of a case of this character is more difficult because the ataxia is not so prominent. . . . In other cases the symptoms indicate an implication first, or at least chiefly, of the upper portion of the spinal cord; the pains in the head, face, and neck are severe, the ocular symptoms develop early, and the pains of the lower extremities diminish and ataxia does not develop until late." The findings in Leyden's case, to which Leyden[5] refers briefly in the above quotation, he said later were very similar to those in Martius' case. The columns of Burdach were the ones chiefly degenerated, while those of Goll were very slightly affected. Leyden, in 1888, said that his own case and Martius' were the only cases of tabes cervicalis with microscopical examination of the spinal cord on record. It will be seen from this that accurate knowledge concerning the symptomatology and pathology of tabes cervicalis dates from 1876, and yet in the past twenty-five years very few cases with necropsy have been reported. I have not been able to obtain the papers containing the reports of the cases of Mayer and Vucetie.

[1] Nothnagel's Specielle Pathologie und Therapie, vol. x. p. 508.

[2] Die Pathologie der tabischen Hinterstrangserkrankung, 1897.

[3] Obersteiner's Arbeiten, 1892, vol. i. p. 26.

[4] Klinik der Rückenmarkskrankheiten, zweite Band, zweite Abtheilung, p. 350.

[5] Deutsche med. Wochenschrift, 1888, vol. xiv., No. 9, p. 164.

In 1888 four cases of cervical tabes, two of which were with necropsy, were published. They were those of Weir Mitchell, Dejerine, Martius, and Bernhardt. Weir Mitchell[1] described a case of cervical tabes without necropsy in which the knee-jerks were excessive on each side.

In Dejerine's[2] case of superior tabes the disease began with impairment of vision and diplopia. Both optic nerves became atrophied and myosis was present. Lancinating pains were felt in the upper limbs and in the back part of the head and in the trunk and thighs. The movements of the upper limbs became so impaired from ataxia that the man had little use of those parts. Walking was difficult, simply because he could not see well, but the movements of the lower limbs were not ataxic. Tactile and pain senses, but not temperature sense, were much retarded in the upper limbs and face, and less so in the trunk. Sensation was almost normal in the lower limbs. The muscular sense was lost in the upper limbs, but preserved in the lower limbs. The olecranon reflex was lost, but the patellar reflex was preserved in the adductors of the thighs, although the jerk of the knee was absent. Romberg's sign was not present. Taste, smell, and hearing were preserved. No visceral disturbances existed. The cerebrum and cerebellum were found to be normal, the posterior roots were much degenerated in almost the entire cervical region and upper part of the thoracic region, and very slightly so in the lumbar region. Slight posterior leptomeningitis existed. The anterior roots were normal. The spinal root of the fifth nerve was much degenerated on each side. Both sixth nerves were degenerated. The posterior columns were much degenerated in the cervical region, less so in the mid-thoracic region, and very slightly so in the lumbar region. Slight alteration of Clarke's column was observed. The anterior part of the spinal cord and the nuclei of the cranial nerves were normal.

In the case of cervical tabes reported by Martius the disease began with paræsthesia in the upper limbs, especially in the hands and fingers, and later similar paræsthesia was experienced in the lower limbs, with weakness of those parts. Ataxia could not be detected. The man was unable to distinguish objects by touch when his eyes were closed, and he had some disturbance of pressure and temperature senses. Romberg's sign, Argyll-Robertson's sign, and Westphal's sign were absent; indeed, the knee-jerk was easily obtained on each side and without reinforcement. Still later girdle sensation was felt. The patient died from pneumonia in the same year that his symptoms were studied, but during the pneumonia reflex rigidity of the iris was detected. The knee-jerk was present until death. The degeneration of the posterior columns was most intense in the cervical region, and was very slight in the lumbar region, and Westphal's root entrance zone was fully intact.[1]

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[1] Medical News, April 21, 1888.

[2] Archives de Physiologie, 1888, 4 Série, Tome i. p. 331.

Bernhardt's[2] case of cervical tabes was without necropsy. The knee-jerks were absent and the ataxia was very pronounced in the upper limbs but not in the lower.

In Eichhorst's[3] case the posterior columns were degenerated in the cervical and upper two-thirds of the thoracic region. The posterior columns in the lower third of the thoracic region and in the lumbar and sacral portions were not affected, and yet the knee-jerks were lost. Leyden believed that loss of the patellar reflex might occur in tabes from neuritis, but Eichhorst was the first to actually demonstrate in the report of this case that the loss may be so produced. He found intense neuritis of the crural nerves. It is interesting to know that while in this case the posterior roots of the lumbar region were not degenerated, the more peripheral parts of these neurons were greatly altered.

In the case of superior tabes reported by Marinesco the degeneration in the columns of Burdach was distinct at the third cervical segment, and on one side the posterior roots were degenerated as high as this level. The degeneration of the posterior roots extended downward as far as the seventh thoracic segment. The posterior roots were not altered in the lumbar region, but in the cervical the degeneration of the columns of Burdach was intense, much more so than in the case I have studied. The patient had had ocular palsies, impairment of vision, pain in the right shoulder, partial paralysis of the right upper limb with anæsthesia and analgesia of this limb extending to the thorax on the same side, masque tabétique (Charcot), and loss of sensation in the conjunctiva and cornea. There was no disturbance of the muscular sense. The patellar reflex was preserved. The pupils were equal, somewhat contracted, and the irides did not react to light or accommodation. The visual fields were contracted. The oculomotor nerve was paralyzed on each side. The bulb does not appear to have been examined. In the atlas in which this case is published Marinesco[4] gives a picture of a section from the cervical cord from another case of cervical tabes, and in this case the tabetic degeneration was in an early stage.

In both the cases reported by Redlich[5] the degeneration of the posterior roots was not confined to the cervical region. In his second case the "local tabetic degeneration"—by which he refers to the degeneration of the posterior roots at their entrance into the spinal cord—began in the upper part of the thoracic cord and extended as high as the upper cervical region.

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[1] Deutsche med. Woch., 1888, No. 14, p. 163.

[2] Zeitschrift für klin. Med., 1888.

[3] Virchow's Archiv, 1891, vol. cxxv. p. 25.

[4] Atlas der Pathologischen Histologie des Nervensystems. Victor Babes. v. Lieferung, 1896.

[5] Die Pathologie der tabischen Hinterstrangserkrankung, 1897. Obersteiner's Arbeiten, 1892. vol. i. p. 26.

In the case diagnosticated as one of cervical tabes by de Buck,[1] weakness, ataxia, lancinating pains, and objective disturbances of sensation were present in the upper limbs. The gait was slightly ataxic and Romberg's sign was present. The Achilles reflex was absent on each side, but the patellar reflex was exaggerated on each side. I am not aware that any case of cervical tabes with exaggerated knee-jerks and necropsy has ever been reported, so that we are in complete ignorance of the cause of this exaggeration. De Buck's case was merely a clinical one.

It is not to be supposed that I have included all the clinical cases of cervical tabes. Some are alluded to in a cursory manner. Mott,[2] for instance, refers to one of his cases in which the cervical tabes began in the upper limbs of a mounted policeman, and infers that the greater use of the upper limbs was the cause of this unusual involvement.

Dr. Cohen's case was one of bulbar tabes as well as one of cervical tabes. Bulbar disturbances as a part of the tabetic symptom-complex are not common, although paralysis of the ocular muscles, either transitory or persistent, has been observed not infrequently. Leyden and Goldscheider[3] have found that paralysis of the external ocular muscles occurs in about 40 to 50 per cent. of the cases of tabes, and that paralysis of the external rectus is the most common of these. In Dr. Cohen's case there was distinct paresis of the right external rectus and partial degeneration of the extramedullary portion of the right sixth root near the medulla oblongata. Paralysis of the facial or of the motor portion of the trigeminus is rare, although Peterson and Schultze have each reported a case of paralysis and atrophy of the muscles of mastication in tabes. Leyden,[4] in 1876, said that unilateral facial paralysis sometimes occurs in tabes, but is incomplete and transitory. Hirt[5] regarded facial palsy as such a rare sign of tabes that when it occurs he thought one should consider carefully whether it were not a complication. He observed it in only two out of 345 cases of tabes. Chvostek,[6] in reporting a case of tabes with sensory and motor disturbances in the distribution of the trifacial nerve, difficulty in deglutition, palsies of external ocular muscles, and paralysis of the right facial nerve in the lower part of its distribution, refers in refutation of Hirt's opinion to the cases of Fournier, Kahler, Semon, Dejerine, Peterson, Jeoffroy-Hanot, and Ehrenberg.

In all three of the cases of tabes with bulbar symptoms reported by Cassirer and Schiff disturbances in the lower distribution of the facial nerve were observed, but there were no central changes to explain these symptoms.

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[1] Journal de Neurologie, June 20, 1899, No. 13, p. 241.

[2] Lancet, July 14, 1900, p. 87.

[3] Nothnagel's specielle Pathologie und Therapie, vol. x. p. 532.

[4] Klinik der Rückenmarkskrankheiten, zweite Band, p. 344.

[5] Pathologie und Therapie der Nervenkrankheiten, second edition, p. 529.

[6] Neurologisches Centralblatt, 1893, No. 12, p. 762.

In Peterson's case of tabes the weakness and atrophy of the masseter and temporal muscles were pronounced, and in eating the man had to support and assist the lower jaw with his hands. The two pterygoids on each side were paretic. There was no anæsthesia of the face. The left side of the face was a little paretic, the action of the occipitofrontalis was stronger and the nasolabial fold deeper on the right than on the left side.[1]

The facial implication seems, therefore, to have been slight. In Dr. Cohen's case the findings in the seventh nerves and their centres do not afford a satisfactory explanation of the facial paresis, and it is possible that it was the result of disturbed muscular sense from degeneration of the fifth nerves.

Hemiatrophy of the tongue in tabes seems to have been first observed by Charcot and later by G. Ballet. When Koch and P. Marie[2] reported their case they could find only five other cases of hemiatrophy of the tongue occurring in tabes, and only two others with microscopical examination (Raymond and Artaud, Westphal, Koch and Marie). In these three cases the twelfth nucleus on the side corresponding to the atrophied side of the tongue was degenerated. Marie later refers to a case with necropsy reported by Mathias Duval. Cassirer and Schiff refer only to the cases of Raymond and Artaud, Koch and Marie, Westphal, and Eisenlohr, as cases of tabes in which either unilateral or bilateral degeneration of the nucleus of the hypoglossal nerve had occurred, and in all these cases except Eisenlohr's the atrophy of the hypoglossal nucleus was unilateral. In a case of tabes reported by Cassirer and Schiff the hypoglossal nuclei in the greater portion of their extent were normal, but in the distal portion of the nucleus on the side corresponding to the atrophy of the tongue there was a very slight diminution in the number and size of the nerve cell bodies. They regarded this alteration as insufficient to explain the atrophy of the tongue, and they believed the atrophy of the tongue was produced by degeneration of the hypoglossal nerve. In the case I have examined the hypoglossal nucleus in its inferior portion on the side corresponding to the half of the tongue at first most atrophied was much smaller than the corresponding nucleus of the other side, and Cassirer and Schiff's observation may have more importance than they attribute to it.

It is my belief that if the medulla oblongata were studied more frequently in cases of tabes, degeneration of the spinal root of the trigeminal nerve would not be a very rare finding. I have seen it in a number of cases of tabes. According to Cassirer and Schiff, the degeneration of this root was first detected by Westphal in 1864, and later by Oppenheim and Siemerling, Hayem, Flechsig, Vulpian, and others. Cassirer and Schiff found the spinal root of the trigeminus degenerated in three cases of tabes, and in one of these the degeneration was unilateral. They point out that in some cases the root was more degenerated in its inferior than in its superior portion (Oppenheim and Siemerling, Eisenlohr, Zeri), and that in others the dorsal part of the root or the ventral part was most degenerated. In the case I have studied as well as in those of Cassirer and Schiff the glia cells seemed to be more numerous in the degenerated spinal roots. In their cases the sensory nucleus of the trigeminal nerve was perfectly normal, as it was at least on one side in my sections, although in cases reported by others it has been found degenerated. The sensory disturbances in the face that have been observed in cases in which the spinal root of the fifth nerve was found degenerated were not always the same, but Cassirer and Schiff say that in their cases sensory disturbances were always present in the face when the spinal root was greatly degenerated, although a parallelism between the clinical signs and the pathological findings was not present. We shall probably not err if we attribute to the degeneration of the spinal root of each fifth nerve, in Dr. Cohen's patient, the disturbance of sensation in the face, possibly the loss of taste on the anterior portion of the tongue, and even at least some of the motor bulbar symptoms, explaining these as a result of loss of sensory impulses.

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[1] Journal of Nervous and Mental Disease, 1890, vol. xvii. p. 450.

[2] Revue de Médecine, 1888, vol. viii. Vorlesungen über die Krankheiten des Rückenmarkes, p. 283.

In one of his cases of tabes, Oppenheim[1] says paræsthesia and disturbance of function were observed in the distribution of the fifth nerve. The patient's face felt stiff, and he had paræsthesia in the mouth and tongue and difficulty in chewing and swallowing, and yet this difficulty was not caused by disturbance of motor nerves or, at most, very slightly so, as the muscles of mastication were powerful and paresis of the soft palate was very slight. Ataxia of the muscles of the face and tongue and of mastication became so great that when the patient attempted to speak he showed great contortion of the face. All these disturbances were probably the result of alteration of the fifth nerve. In another case in which implication of the fifth nerve existed, chewing and swallowing were difficult, the patient did not know whether any food were in her mouth, and she could extend the tongue properly only when she watched the movements of the tongue in a looking-glass. In both these cases the spinal root of the fifth nerve was degenerated on each side.

Oppenheim says that Duchenne spoke of implication of the fifth nerve in tabes. He also says that the symptoms attributed to degeneration of the spinal root of the fifth nerve have varied considerably in different cases.

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[1] Arch. für Psychiatrie, 1888, vol. xx. p. 131.

The constant biting of the cheeks, for the relief of which in 1886 Dr. Cohen's patient had several teeth extracted, and the absence of pain upon their removal, as well as the loss of food in the mouth, were probably the result of degeneration of the spinal roots of the fifth nerves.

The descending root of the vago-glossopharyngeus is occasionally found degenerated in tabes. Cassirer and Schiff collected twelve cases in which degeneration of this bundle was observed, but only in six of these was the microscopical examination thorough. The absence of disturbance of taste in these six thoroughly studied cases seems to show that integrity of the solitary bundle is not necessary for the function of taste. Disturbances of the functions of the larynx observed in these six cases were not necessarily the result of degeneration of the solitary bundle, because there was also degeneration of the bulbar nuclei or of the peripheral portions of the vagus and glossopharyngeus nerves. In one of the twelve cases the solitary bundle was degenerated, but clinical signs indicative of this degeneration had not been observed. Cassirer and Schiff conclude that the solitary bundle has no relation to the function of taste, or of sensation or motion in the larynx, or to deglutition. The degeneration of this bundle has no relation to gastric crises or disturbances of respiration. Cassirer and Schiff found the large fibres in the solitary bundle degenerated, while the fine fibres were preserved and formed a group on the dorso-median portion of the bundle. In Schlesinger's[1] case both descending glossopharyngeal roots were degenerated, and, according to Schlesinger, the degeneration of these roots has been found in tabes especially when laryngeal disturbances had been present, and yet he merely calls attention to the frequency of the association without expressing himself very positively in regard to the importance of it. It seems from his investigations, also, that degeneration of these roots does not cause disturbance of taste.

It is possible, however, that the feeble and irregular cardiac action in Dr. Cohen's patient was the result of the degeneration of the descending root of the left vago-glossopharyngeus.

The dorsal nucleus of the vagus has been found degenerated in tabes, and was so in one of Cassirer and Schiff 's cases, but these authors were unable to observe positive degeneration of the nucleus ambiguus, and I also have been unable so to do in the sections studied by me.

Cases of bulbar tabes with necropsy are very rare, and v. Reusz,[2] in publishing a case of this kind, says only two other such cases have been reported since the appearance of the paper by Cassirer and Schiff, viz., a case by Grabower and Oppenheim and one by Zeri, but the case by Zeri is probably referred to by Cassirer and Schiff.

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[1] Wiener klin. Wochen., 1894, No. 27, p. 497.

[2] Archiv f. Psychiatrie, 1899, vol. xxxii., No. 2, p. 535.

A CASE OF COMPLETE ABSENCE OF THE VISUAL SYSTEM IN AN ADULT.[1]

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(From the William Pepper Laboratory of Clinical Medicine, Phoebe A. Hearst Foundation.)

Complete absence of the visual system is of very rare occurrence, especially in an adult. The study of the case I report in this paper should be of more value than one of agenesia of the visual system in a newborn child, because in the latter portions of the brain not belonging to the visual system are imperfectly developed, and faulty conclusions may therefore be drawn.

The boy, T. S., according to the case-books of the Pennsylvania Training School for Feeble-minded Children, was born in 1878, and was admitted to the school March 12, 1895. At the time of admission he weighed thirty-eight pounds, and his height was three feet seven inches. He was an idiot, absolutely helpless, and very unclean. He could say "mamma," and nothing more. He was passionately fond of music. At the time of admission to the school he appeared to be about eight or ten years of age.

I saw him on July 30, 1897, and made a few notes on his condition. I regarded the case at that time as one of cerebral spastic paraplegia of the lower limbs, with absence of the eyeballs. The boy was unable to stand alone, and if he were stood up and not supported he fell backward. When supported he could take a few steps, but in doing so one lower limb was moved in front of the other (cross-legged progression). His knee-jerks were exaggerated, but ankle clonus was not obtained. He could move his lower limbs while he was sitting, and there was not excessive rigidity of these limbs on passive motion. He uttered only a few monosyllables. His palpebral fissures were very small. He died March 2, 1900, and the necropsy was made two days later. The necropsical notes I shall use only in so far as they are of importance for the understanding of the case.

The body was that of a child apparently about twelve years of age (see Fig. 1), though in reality his age was twenty-two years. No signs of puberty were present. The testicles were not in the scrotum; the right testicle, quite small, was found in the inguinal canal just above the pubes. The genitalia were like those of a child of ten years. No hairs were found on the pubes, or in the axillæ, or on the face. The circumference of the head was eighteen and three-fourth inches; the length of the body was forty-seven inches. The right upper limb could not be fully extended at the elbow, while the left upper limb could be fully extended. Slight contracture of the fingers of each hand was observed, so that the fingers could not be fully extended when the hands were fully extended at the wrists. The fingers could be fully extended when the hands were flexed at the wrists, as the contracture of the flexors of the fingers did not then interfere with the extension of the fingers. The lower limbs were slightly flexed at the knees, and could not be fully extended.

The palpebral fissure of each eye was very small, and the orbits contained only a small amount of what appeared to be fibrous connective tissue. Unfortunately, permission had not been given for the removal of the orbital contents. Nothing resembling an eyeball was seen.

The optic foramina did not exist, and it was impossible to find an opening in the usual situation of these foramina, and here there were merely slight depressions in the skull. No trace of optic nerves, chiasm, or optic tracts could be found. (See Fig. 2.) There was no sign of an external geniculate body on either side, and the thalamus on each side had nothing resembling an optic tract passing from it. The posterior part of each thalamus was rounded and larger perhaps than one would expect to find it in a case of complete agenesia of the visual system. (See Fig. 3.) The brain was small, firm, and not edematous. The left ascending frontal convolution in the centre for the upper limb was very small (see Fig. 4), to which fact possibly was due the contracture of the right forearm (see Fig. 1), because of imperfect development of the nerve fibres innervating this limb. The anterior colliculi of the corpora quadrigemina were fully as large and as well developed as the posterior. The occipital lobes were small, and the cuneus on each side (see Fig. 5) was small and the calcarine fissure short. The lower olives were covered by thick bands of nerve fibres—*i. e.*, the external arcuate fibres were unusually well developed.

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[1] Read before the College of Physicians, November 6, 1901.

The spinal cord was small, but not otherwise abnormal.

The brain was hardened in formalin, and the basal ganglia of one hemisphere were cut in serial sections, while those of the other hemisphere were preserved intact as a gross specimen. Sections were made through the cortex of the left calcarine fissure, and stained by thionin and by Weigert's hematoxylin method. Frontal sections were made through the right occipital lobe in order that the optic radiations might be studied when cut transversely. The nerves supplying the ocular muscles were also cut and examined.

The cortex of the left calcarine fissure stained by thionin contained many nerve-cell bodies, but they were possibly slightly less numerous than are the cell bodies in sections from the corresponding region of a normal brain, especially in the third, fourth and fifth layers. The giant cells of the third layer were represented, but were possibly not as numerous as in a normal brain. The fibres of Vicq d'Azyr of the cortex of the calcarine fissure were not very distinct in sections stained by Weigert's hematoxylin method, but they were not entirely absent.

The optic radiations in the frontal sections of the occipital lobe were not entirely absent, but the area occupied by them was not very distinct.

Meynert's commissure was normal, and stained well by Weigert's hematoxylin method. (See Fig. 6.)

Careful examination of the serial sections failed to show the slightest trace of an external geniculate body on either side, although the internal geniculate body was well developed. Fig. 6, a photograph from one of the sections, shows the internal geniculate body in its normal size, as well as the inferior posterior portion of the optic thalamus, but the external geniculate body, which should be present in a section at this level, is entirely absent. Comparison with Fig. 326 of the *Anatomie des Centres Nerveaux*, Vol. I, by J. and A. Dejerine, is instructive. This drawing is from a section cut in the same direction as that represented in Fig. 6 of my series, and shows the normal size of the external geniculate body and an optic tract in a section from this level. In the section of my series represented in Fig. 6 there is no trace of an optic tract.

Some few medullated nerve fibres are found within the pulvinar in my section, but those in the posterior portion of the thalamus are much fewer than those in the more anterior portions. The contrast is very striking, and is represented in a drawing of a horizontal section (see Fig. 7), which should be compared with a corresponding section from a normal brain, as shown in Fig. 321 of the *Anatomie des Centres Nerveaux*, by J. and A. Dejerine.

The habenula in the horizontal sections appears well developed, and the fasciculus retroflexus of Meynert is well stained.

In the photograph the anterior colliculi of the corpora quadrigemina appear smaller than the posterior; but this is merely because the former were further from the camera.

Sections through one-half of the oculomotor nuclei stained with thionin contain many nerve-cell bodies belonging to these nuclei, and these cell bodies stain well with thionin and appear to be normal. They are possibly not as numerous as cell bodies in oculomotor nuclei of a normal brain. Sections through one-half of the oculomotor nuclei were also stained by the Weigert hematoxylin method.

Transverse sections of the extracerebral portion of the left oculomotor nerve near the cerebral peduncles stained with ammonium carmin show an apparently normal nerve. The nerve is possibly smaller than an oculomotor nerve from a normal brain, but it contains no sclerotic areas. It contains, however, some areas in which very fine nerve fibres form distinct groups, but there is no scarcity of large nerve fibres.

Transverse sections of the right oculomotor nerve are very similar to those of the left oculomotor nerve. The sections stain well by Weigert's hematoxylin method.

One of the trochlear nerves in transverse sections, stained either by ammonium carmin or Weigert's hematoxylin, appears to be normal, and contains nerve fibres of good size. The nerve fibres stain well with the Weigert hematoxylin, but in sections so stained the nerve fibres are perhaps not quite so close together as in the trochlear nerve from a normal brain.

The nerve fibres of the left abducent nerve stained in transverse sections by acid fuchsin are exceedingly small, much smaller than those of the oculomotor and trochlear nerves, but they stain well with Weigert's hematoxylin.

The right abducent nerve in transverse sections stained by acid fuchsin contains many nerve fibres that are much larger than any of those found in the left abducent nerve, but it contains also many sclerotic areas. Some of the nerve bundles stained by Weigert's hematoxylin method contain very few medullated nerve fibres. The contrast between the abducent nerves and the other two ocular nerves on each side is most striking. (See Fig. 8.)

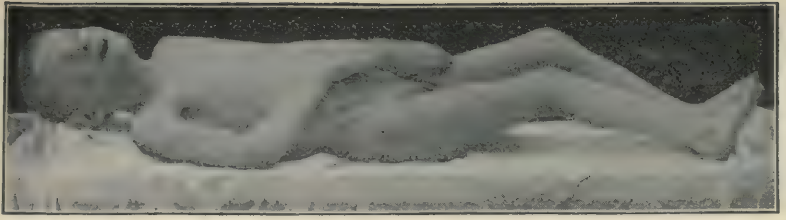

Fig. 1.—A photograph of T. S., taken after death. The right upper limb, the fingers of both hands, and the lower limbs are slightly contractured. The palpebral fissures are small.

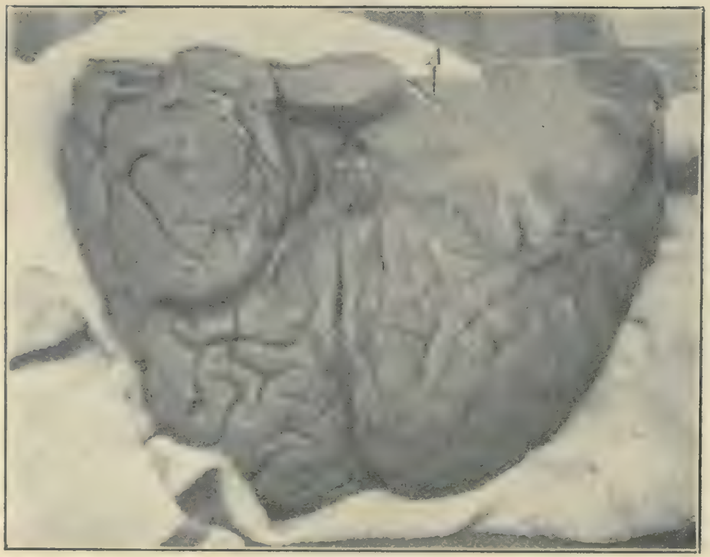

Fig. 2.—The occipital lobes have been cut away. A portion of the right temporal lobe has also been cut away in order to show the complete absence of the visual system. The internal geniculate body (A) is well shown, but no trace of the external geniculate body or of an optic tract or chiasm can be found.

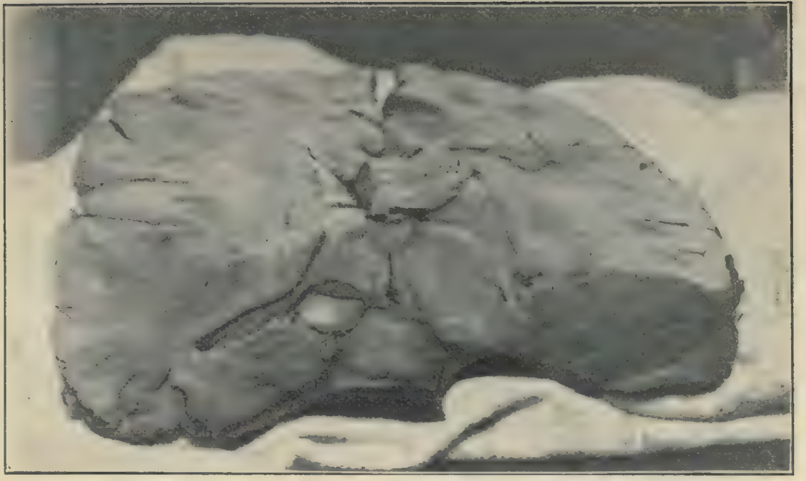

Fig. 3.—The optic thalami are well shown. The anterior colliculi of the corpora quadrigemina, especially the right colliculus, appear smaller than the posterior, because the former were further from the camera.

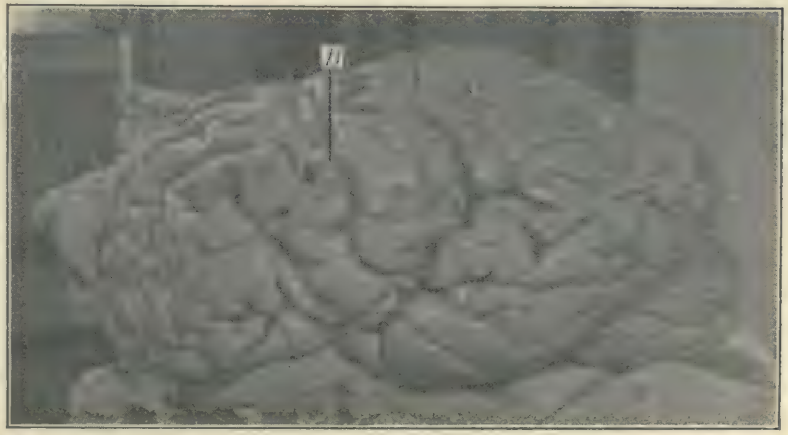

Fig 4.—The left ascending frontal convolution in the centre for the upper limb (B is very narrow.

The nucleus of each abducent nerve contains many nerve-cell bodies, which, with the thionin stain, appear to be normal.

The nerve-cell bodies of the anterior horns of the spinal cord in the cervical and lumbar regions stained with thionin are normal, but possibly a little smaller than those usually present in the anterior horns. No sclerotic areas are found in the lateral columns, neither are the nerve fibres in these columns unusually fine in transverse sections.

Von Monakow gives as primary optic centres the external geniculate body, the surface of the pulvinar, and the superficial gray matter of the anterior colliculi of the corpora quadrigemina. He says that Stilling, Bernheimer and Kölliker believed that visual fibres arise also in the hypothalamic body, the internal geniculate body and the tuber cinereum. The anterior colliculi of the corpora quadrigemina in man, according to his view, have a very subordinate rôle in vision, and he believes that about 80 per cent of the optic-nerve fibres terminate in the external geniculate body. My case of congenital absence of the central visual system confirms these views of von Monakow. It shows also that Meynert's commissure and the habenula are not part of the visual system. According to von Monakow (*Gehirnpathologie*), centrifugal fibres—*i. e.*, fibres having their origin in the visual cortex—are present in the optic radiations and pass to the inter-brain and mid-brain. The giant pyramidal cell bodies of the third layer in the cortex of the occipital lobe give off axones, which pass by way of the optic radiations and the arm of the anterior colliculus of the corpora quadrigemina, to terminate in the superficial medullary substance and gray matter about the aqueduct of Sylvius in the anterior colliculus. The Vicq d'Azyr fibres, he says, are often in a double row in the occipital lobe. They come, in greater part, from the fibres of the optic radiations which pass to the third layer of the cortex, but some of the Vicq d'Azyr fibres may belong to an association system. In long-standing lesions of the optic radiations the Vicq d'Azyr fibres are very atrophic, and the double row of these fibres is scarcely recognizable. In my sections the comparatively few fibres passing to the pulvinar are doubtless the fibres described by von Monakow as arising in the occipital lobe, and in my sections the Vicq d'Azyr fibres are not very distinct.

Von Leonowa has examined the microscopical sections from four cases of anophthalmia and three cases of atrophy of the eyeball, but in all these death occurred within a few months after birth. In all her cases the posterior colliculi of the corpora quadrigemina were intact, but the anterior colliculi were affected. Von Leonowa[1] concludes from a study of the cases mentioned above that the posterior colliculi of the corpora quadrigemina have no relation to vision, while the anterior have; that the relation of the external geniculate body to the visual fibres is a very intimate one; and that the hypothalamic body has no relation to vision. In none of her cases was the absence of the visual system complete, and all the brains were from children in the early periods of extrauterine life.

In her cases the nuclei of the third, fourth and sixth cranial nerves were intact, and this integrity is explained by von Leonowa as a consequence of the existence of ocular muscles. The external ocular muscles may be well developed, even though the eyeballs are exceedingly atrophic, as in a case of anophthalmia in a person of twenty-seven years, reported by Haab, in whom the ocular muscles were normal in size and shape, although the ocular bulbs were very small. The nerves to the ocular muscles need not be absent in congenital defect of the visual system. In my case there was apparently no eyeball on either side, but in the small amount of fibrous tissue at the posterior portion of each orbit muscles may have existed, even though they had little or no function. One might suppose that in the case I have reported the third, fourth and sixth nerves would have been very imperfectly developed in conformity with the law of Gudden, according to which atrophy in a neurone follows injury to this neurone. It should be remembered, however, that in my case the ocular nerves were not injured, and may have been in union with ocular muscles, as in Haab's case.

It has been shown by von Leonowa[2] in the report of a much-quoted case that nerve fibres may develop, although they apparently have no function. She examined a fetus in which the brain and spinal cord had not developed, and yet the vertebral canal was filled in its entire extent by posterior nerve roots. Some of the fibres of the posterior roots extended from the lower part of the canal to the upper, as they would have done if they had formed the posterior columns of a normal spinal cord. All the posterior roots ended blindly, and appeared as though they had sought a spinal cord in which to bury themselves. No anterior roots were found. All the peripheral nerve fibres present

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[1] *Archiv für Psychiatrie*, 1896, vol. xxviii, p. 53.

[2] *Neurologisches Centralblatt*, 1893.

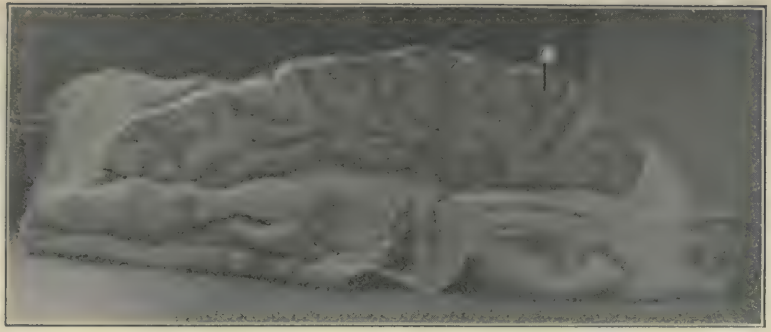

Fig. 5.—The upper part of the right cerebral hemisphere, showing the small cuneus (C).

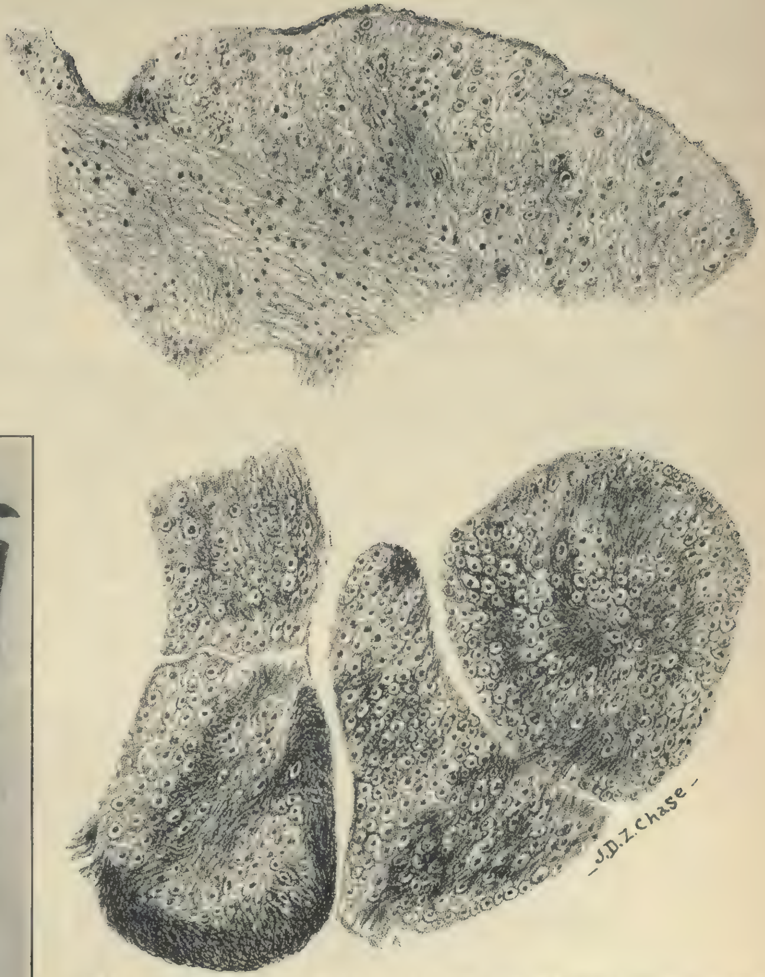

Fig. 8 —Drawings of transverse sections through portions of the abducent nerves. The upper drawing represents the fine fibres of the left abducent nerve, and the lower drawing the sclerotic areas in the right abducent nerve.

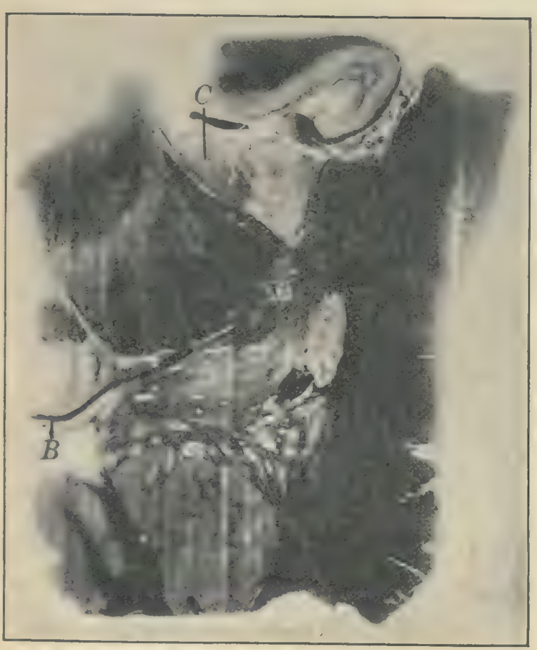

Fig. 6.—Photograph of a horizontal section of one cerebral hemisphere, showing Meynert's commissure (B) well developed, and also the internal geniculate body (C), while the external geniculate body is entirely absent.

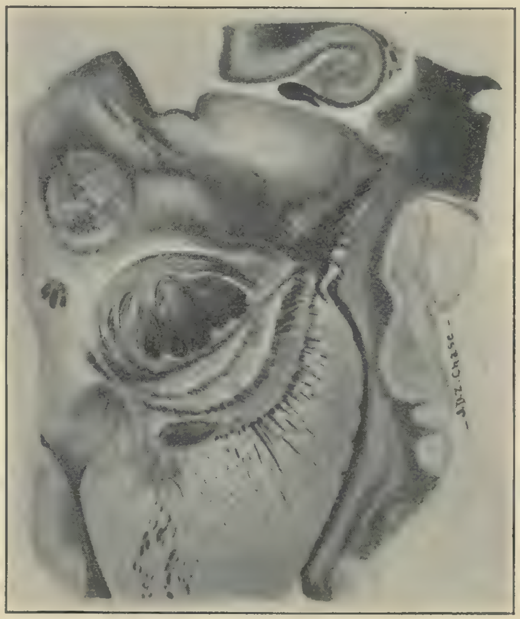

Fig. 7.—A drawing of a horizontal section through the basal ganglia of one hemisphere. The fibres entering the posterior part of the optic thalamus are few in number.

had their origin in the spinal ganglia, and belonged, therefore, to the sensory system. The muscles of the limbs appeared fully normal, although no motor nerves existed. Most of the axis cylinders of the posterior roots were non-medullated or had only a thin medullary sheath. The cell bodies of the spinal ganglia were as numerous and as well developed as in a normal fetus. The absence of medullary sheaths on the posterior roots, von Leonowa thinks, may have been caused by the amniotic fluid, inasmuch as medullary sheaths were present on axones that were covered by the skin.

Gade[1] and Karl and Gustaf Petrén have found posterior roots growing into the spinal canal in complete failure of development of the spinal cord. I am unable to determine from the statements of the latter authors whether in their case or in Gade's the individual fibres of the posterior roots were normal or not.

With the results of these investigations in mind we can understand that nerves might grow equally well into the orbits and persist, even though the ocular muscles were absent. Indeed, von Leonowa and Karl and Gustaf Petrén have shown also that in early life muscles may be developed, although no motor nerves exist, so that the converse may well be true—*i. e.*, motor nerves probably may exist, although the muscles usually supplied by these nerves are not developed. All the ocular nerves in my case, however, were not normal. The two sixth nerves were very imperfectly formed.

Meynert's fibres are asserted by some to be the connection between the optic nerves and the oculomotor centres, although such distinguished cerebral anatomists as Edinger and von Monakow tell us that the anatomical proof for this assertion is wanting. Recent investigations seem to indicate that some of these Meynert fibres (for there are more than one band of fibres named after Meynert) belong to a bundle extending into the anterior columns of the spinal cord. In my case the Meynert fibres in the corpora quadrigemina were well developed, although there could have been no reflex fibres from the iris to the oculomotor centres, so that we must conclude that the function of these Meynert fibres cannot be merely to serve the pupillary reflex. I am unable to give the course of the so-called pupillary fibres from a study of my preparations, as the fibres in the region of the corpora quadrigemina form an intricate network.

It is not surprising that cell bodies should be numerous in the cortex of the calcarine fissure in a case of congenital absence of the visual system. Some of these cell bodies have axones which are situated in the optic radiations and terminate in the primary optic centres—*i. e.*, the external geniculate body, the pulvinar of the thalamus, and to a less extent the anterior colliculi of the quadrigeminal bodies, and these fibres probably are not directly concerned in vision. The visual cortex is intimately connected with widely separated portions of the brain, as shown both by physiological and anatomical investigations. The movements of the limbs, the functions of speech, and especially the movements of the eyeballs, are in intimate relation with vision, and important association tracts between the visual area and other parts of the brain can be demonstrated anatomically. The cell bodies of the visual cortex must have axones in relation with remote parts of the cerebral cortex, and, therefore, it is not surprising that these association neurones are developed even in a case of congenital defect of the visual system. Von Monakow represents in his *Gehirnpathologie* (p. 265) a section of a calcarine cortex from a case of lesion of the optic radiations. The giant pyramidal cell bodies of the third layer of the cortex had entirely disappeared, and the third, fourth and fifth layers were degenerated in a way they were not in my case. It should be remembered that in von Monakow's case axones were destroyed whose cell bodies were situated in the calcarine cortex, and that atrophy of these cell bodies probably followed the injury of their axones. This did not occur in my case, and probably the nerve fibres present in my specimens in the optic radiations arose in the occipital lobe. It is difficult to understand what the function of these fibres can be.

Although the individual described in this paper was an idiot, we should be cautious in attributing his deficient mental development to the absence of his visual system. It would seem probable, however, that the entire brain was in a state of imperfect development.

The spastic paraplegia of the lower limbs deserves mention. The nerve-cell bodies of the anterior horns in the lumbar cord were normal by the thionin stain, except that they were not so large as the cell bodies of this region usually are, and the lateral columns did not contain sclerotic areas. This is not the first time I have found an apparently normal spinal cord in congenital spastic paraplegia, and I think the explanation is to be found in an imperfect development of the motor neurones. A deficiency from birth in the number of these neurones would probably have the same result as partial destruction of the central motor tracts, and in the absence of the development of motor neurones there would be no sclerosis, inasmuch as no space existed to be filled by proliferation of the neuroglia. Indeed, sclerosis may be entirely absent if destruction of nerve fibres occurs in early life, because the growing tissue of the spinal cord fills the space left by degenerated fibres, and proliferation of the neuroglia does not occur. I have seen the spinal cord in a case of infantile hemiplegia presenting little or no sclerosis, although the person from whom this cord was removed had lived many years after the paralysis had developed. The case to which I refer was in Dejerine's service. In two cases of congenital spastic paraplegia of the lower limbs I believed I was able to detect an unusual fineness of the nerve fibres of the pyramidal tracts, but I was unable to do so in this case, T. S.

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[1] Gade, cited by Carl and Gustav Petrén *Virchow's Archiv*, 1898, B. 151.

I am indebted to Dr. de Schweinitz for the reference to a case reported by W. S. Little[1] in 1885, in which congenital absence of some portions of the visual system was found. The brain was from a child of ten years of age, who had been an inmate of the Pennsylvania Training School for Feeble-minded Children, and the specimen was examined by A. W. Wilmarth. This child had had bitemporal hemianopsia. There was no optic commissure, but a small projection was found on the inner side of each nerve where the commissure should have been. These projections did not touch by at least one-quarter of an inch. A complete study of the specimen does not seem to have been made.

A still more important case, and one more closely resembling mine, has been reported by Haab.[2] His specimen was from a girl, twenty-seven years old, who had the development of a child of fourteen or fifteen years, and from her appearance had not reached puberty. She was an idiot, and had much difficulty in walking. The optic chiasm was entirely absent, but the optic tracts were present as small bands. The oculomotorius, abducens, and trochlearis appeared to be normal, and yet the merest trace of an eyeball was found. The muscles of the orbits appeared to be normal. The external geniculate body was entirely absent, but the internal geniculate body was of normal size. The corpora quadrigemina were of normal size macroscopically. The optic foramen was almost obliterated. The pulvinar of the optic thalamus was smaller than in a normal brain.

The conclusions that may be drawn from my case are:

1. The chief "primary" optic centre is the external geniculate body.
2. The pulvinar of the optic thalamus is also an important "primary" optic centre.
3. The anterior colliculus of the quadrigeminal body in man has an unimportant relation to vision.
4. The hypothalamic body, the habenula, the internal geniculate body probably are not part of the visual system.
5. The cortex of the calcarine fissure may contain nearly the normal number of cell bodies, even though the visual system may be undeveloped.
6. The nerves to the ocular muscles and their nuclei may be developed, even though the visual system is absent.
7. Congenital spastic paraplegia may be the result of deficient formation as regards number or size, of the neurones of the central motor system, even though such a deficiency may be difficult to detect by the microscope.

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[1] *Transactions of the American Ophthalmological Society*, 1885, p. 367.

[2] *Beiträge zur Ophthalmologie als Festgabe Friedrich Horner*, 1881, p. 131.

(Reprinted from THE PHILADELPHIA MEDICAL JOURNAL, Feb. 8, 1902.)

THE SENSORY SEGMENTAL AREA OF THE UMBILICUS,

As Determined by a Case of Fracture of the Tenth Thoracic Vertebra, with Complete Compression of the Spinal Cord, and Without Knee-Jerks and Babinski Reflex.

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From the William Pepper Laboratory of Clinical Medicine (Phoebe A. Hearst Foundation).

Operations on the vertebral column, even when no fracture has occurred, have become quite frequent since the publication in 1888 of Gowers and Horsley's famous case of successful removal of a spinal tumor, and therefore reports of cases that add to our knowledge of segment diagnosis are desirable. According to the statement of Boettiger operation has been attempted in thirty-six cases of tumor of the spinal cord. He bases this statement on the statistics given by Putnam and Warren. It is probable that a few recent cases have been omitted in these figures.

Segment diagnosis depends chiefly on motor and sensory conditions, and on electrical reactions. Reflexes are of less importance in this diagnosis, as the same reflexes may be lost in complete lesions at different levels of the cord. Motor paralysis is especially valuable when the condition of the limbs is under consideration, but when the lesion is in the thoracic region of the cord, and the segment diagnosis is sought by the paralysis of the abdominal muscles, the diagnosis may be more difficult. The degree of partial paralysis of the abdominal muscles caused by spinal lesions may sometimes be difficult to determine when these muscles are flabby, as in a woman who has borne many children. It is believed that the motor supply of the abdominal muscles is derived from the ninth thoracic segment to the first

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*Read before the Philadelphia Neurological Society, December 23, 1901.

lumbar segment (Boettiger), so that we may refer the paralysis of the abdominal muscles to these segments of the cord.

Sensory disturbances on the trunk and electrical reactions may be of great assistance in segment diagnosis, but a case that is valuable for this purpose must be one of complete destruction of the spinal cord at one region. As Bruns has pointed out, partial compression of the cord may cause faulty diagnosis, as the sensory nerve fibers compressed and causing the disturbed function may have entered the cord some distance below the seat of compression. Lesions at different levels also may cause confusion in diagnosis.

Boettiger has drawn attention to the value of the electrical reactions of the abdominal muscles in thoracic lesions. These reactions should be determined, if possible, when such lesions exist, because when degenerative change is obtained the level of the lesion may be diagnosticated, especially in connection with other signs.

A case of fracture of a vertebra with complete compression of the cord, followed by necropsy and careful examination, is of much value in spinal localization, because fracture usually gives an area of anesthesia fairly sharply defined at its upper border. This is remarkable, as Sherrington has found that three posterior roots must be cut before complete cutaneous anesthesia can be obtained at any one part, and Bruns places the number at five. In compression of the thoracic cord from fracture of the vertebra we might *a priori* expect the area of anesthesia to shade off gradually at its upper border into the sensory region, but Walton has recently stated that the limitation of the anesthetic zone in such cases is sharp, and this sharp limitation was present in a case with necropsy recently observed by me, and which is reported in this paper, and also in another case of complete division of the cord. It is possible that compression of the spinal cord may cause a more sharply defined area of anesthesia than does compression of posterior roots.

The umbilicus is a very definite point in localization, and the determination of the spinal segment, with which it is in sensory relation, is of importance. Boettiger says it is still uncertain whether the umbilicus lies in the distribution of the ninth or tenth thoracic segment. Walton places it in the distribution of the eleventh thoracic segment, and Dejerine locates it in the distribution of the tenth thoracic segment.

The plates given by Henry Head, showing the distribution of the segmental areas from the first thoracic to the fourth sacral, were made after a study of the appearances presented by the cutaneous tenderness in visceral disease, of a study of the distribution of the eruptions in 62 cases of herpes zoster, and of the limits of analgesia in organic disease of the spinal cord and roots. Head states that he did not suppose that the areas figured by him were absolutely correct, but hoped that future investigations would show that their situation and extent bear a fairly close relation to the truth. The tenth thoracic segment, according to his investigations, represents the subumbilical area, and the upper border of this area, according to one of his plates, passes directly through the umbilicus and appears to be a little more curved downward on each side toward the umbilicus than is the upper border of the umbilical area as given by most authorities.

In a recent paper, Head and Campbell quote Thorburn: "The umbilicus probably lies, not as Head places it at the junction of the ninth and tenth dorsal fields, but certainly no higher than the lowest part of the tenth", but Head still adheres to his opinion expressed in 1893 that the umbilicus lies between the ninth and tenth thoracic areas.

Ralf Wichmann states that the umbilicus lies in the area of the tenth thoracic zone. He quotes Paterson as placing it between the tenth and eleventh thoracic areas; and Kocher as placing it at the lower border of the tenth thoracic segment. In Wichmann's plate the umbilicus is represented as lying in the center, from above downward, of the tenth thoracic zone, and the upper border of this zone is represented more nearly horizontal than it is by Head.

W. Seiffer says that the umbilicus is generally regarded as situated within the tenth thoracic segment, although Head believes it lies between the ninth and tenth segments. To be on the safe side in his scheme of the segmental sensory distribution, Seiffer draws a line from the umbilicus a little downward and then upward and around the trunk, and calls this the umbilical line, and regards it as indicating the tenth thoracic segment. Should further study, he says, show that Head is right, the umbilical line is to be regarded as the border between the ninth and tenth segments. Posteriorly this umbilical line is represented in Seiffer's figure 15 as nearly horizontal.

My case reported in this paper is in confirmation of Head's views, but I have not found the slight concavity in the umbilical line on each side of the umbilicus which Head represents.

My case, as well as others, fully confirms Seiffer's statement that the sensory segmental areas on the trunk are not paralled to the ribs and have no relation to the intercostal spaces, but are in bands whose borders are not fully horizontal.

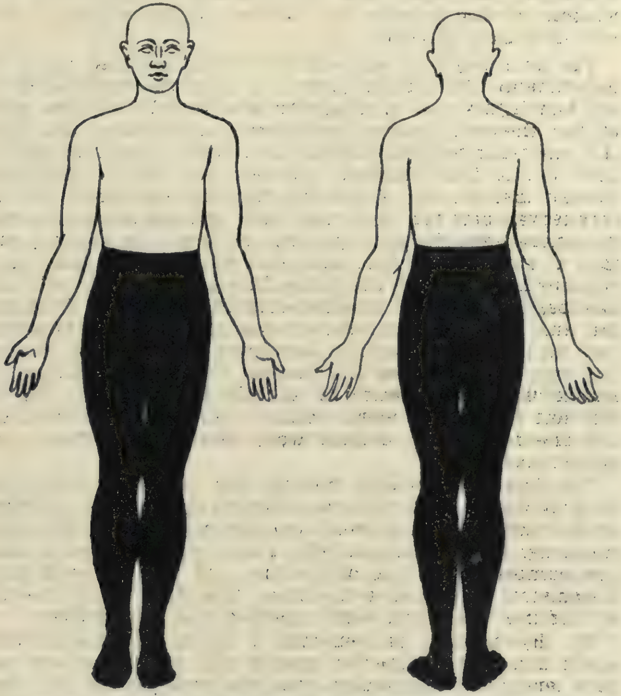
During the past summer I had the opportunity to study a case of fracture of the tenth thoracic vertebra with complete compression of the cord, and to determine the region of the spinal cord destroyed. The case is of value in regard to the segmental zone in which the umbilicus lies, because neither the spinal cord nor roots were implicated at the ninth thoracic segment, whereas the tenth thoracic segment of the cord was much softened. It was therefore a very valuable case for determining exactly in which sensory distribution the umbilicus lies, and was confirmative of Head's opinion that the umbilicus lies between the ninth and tenth thoracic areas.

G. P., a colored man, was admitted to the nervous wards of the Philadelphia Hospital, in my service, June 27, 1901. He stated that about three weeks previously he had fallen a distance of 30 feet and had been picked up and carried to the Jefferson Hospital. He was unconscious after the accident for several days. When he regained consciousness he was unable to move his lower limbs, and had only a little power in his left upper limb. The right upper limb he could move freely. He had pain in his back and in the left shoulder. At first he could hold his urine and pass it when he wished, but at the time he came under my observation he had no power over the bladder and did not know when the urine escaped. Immediately after the accident he had had control over the bowels, but he had lost this control and did not know when his bowels acted.

At the time of my first examination, July 1, 1901, he was completely paralyzed in the lower limbs. He was unable to move a muscle in these limbs even with the greatest exertion. These limbs were flaccid, and no contractures had developed. The knee-jerk on each side was entirely lost and attempts to produce a knee-jerk caused much pain in his back. The Achilles jerk was lost on each side. The Babinski reflex was not obtained on either side. Irritation of the sole of the foot produced no movement of the toes.

The cremasteric reflex was not obtained and priapism was not observed.

The dynamometer, lower scale, in the right hand, registered 10; in the left hand *nil.* He moved the right upper limb freely, and there was very little impairment of motion in this limb. Resistance to passive movement in the right upper limb was normal. He raised the left upper limb at the shoulder and bent it at the elbow fairly well, but was unable to straighten the fingers of the left hand. He was able to make a fist with either hand, and the flexor power in each hand was normal. It was difficult to open the fingers of the left hand. The weakness in the upper extremity was probably the result of muscular injury, as he had been fastened to the bed while he was in a condition of motor excitement after the accident.



FIGS. 1 and 2.—Thedark portion represents the anesthetic area. This area was defined by a line passing directly through the umbilicus, and was a little higher on the right side than on the left.

Sensation for pain and touch was completely abolished over the lower limbs and trunk as high as a horizontal line passing directly through the umbilicus. Above this line sensation for pain and touch was sharply felt. The line dividing the anesthetic area from the sensitive area was a sharp one, but was not absolutely horizontal on the right side, as over the right hip it was one inch above a horizontal line through the umbilicus, but on the left side the line seemed absolutely horizontal. In the middle of the back this line of anesthesia extended about ½ inch above the level of the umbilicus.

The urine contained pus cells and albumin in considerable quantity. The temperature was irregular and reached as high as 104°.

A diagnosis of complete interruption of the spinal cord in the lower thoracic region, probably at the tenth or eleventh segment, from fracture of the vertebral column was made, but, as the condition had existed three weeks and the symptoms of complete compression had persisted without alteration, operation was not considered advisable. The wisdom of this decision was shown by the necropsy. The man died July 14, 1901.

The necropsy was made by Dr. Simon Flexner, and I am indebted to him for his notes. A scar, the remains of an old injury, 4.8 cm. in diameter was found over the spine of the eleventh thoracic vertebra and extended also over the tenth and twelfth thoracic vertebrae. The spinous process of the 10th thoracic vertebra was driven downward against the process of the 11th thoracic vertebra. The interval between the 10th and 11th spinous processes was increased. Beginning 5 millimeters from the superior surface of the spine of the tenth thoracic vertebra was an irregular fracture line extending laterally on each side and passing through the corresponding laminae. The right lamina was prominent and showed the chief injury. The fracture on this side extended downward and forward through the entire diameter of the lamina. The tissues about the lamina were edematous and slightly hemorrhagic. On the left side the tissues were involved to a slighter extent, but the remains of hemorrhage were found in the fascia and spinal muscles.

The fracture extended through the upper portion of the body of the tenth thoracic vertebra so that the two portions of the vertebra moved freely on one another, and the upper fragment was displaced. The spinal cord was completely compressed at the line of fracture and was softened for a distance of 4 cm. above this line. The dura below the line of fracture was much more injected than that above.

By microscopic examination I found the spinal cord much disintegrated in the lumbar and sacral regions, and here round-cell infiltration was observed within the cord, meninges, and anterior and posterior spinal roots. The spinal roots were much degenerated and congested. Blood pigment and swollen axones were found in the sections. The cord contained much amorphous tissue and fatty granular cells, the latter being especially well shown by the Marchi stain. The nerve cell bodies of the anterior horns did not appear to be normal, but they could not be studied by the Nissl method, and the degree of alteration was not therefore accurately determined. Above the area of compression the degeneration in sections from the upper thoracic region was confined to the posterior columns, especially to the columns of Goll, and was slight in those of Burdach; and to Gowers' tracts, the direct cerebellar tracts and the region along the anterior fissure on each side.

In this case the upper border of the anesthetic area passed directly through the umbilicus as represented in Figs. 1 and 2, and was nearly horizontal.

The absence of the Babinski reflex, notwithstanding the implication of the central motor tracts, is probably to be explained by the softening of the cord below the area of compression, and the case shows that where the spinal cord is disorganized in the lumbar and sacral regions, the Babinski reflex may be absent, even though the central motor tracts are diseased.

Much has been written on the loss of the deep reflexes as a result of complete or nearly complete transverse lesion above the lumbar region. My case was one of fracture of the tenth thoracic vertebra with loss of the tendon reflexes, and the fracture was therefore above the area of the cord through which the reflex arc for the patellar reflex passes. The explanation for the absence of the patellar reflex was readily found at the necropsy. The cord below the seat of fracture was softened from a cutting-off of the blood supply and inflammatory changes. A case of transverse lesion of the spinal cord with lost tendon reflexes can be of little value in determining the cause of this loss unless the lumbar region is studied microscopically, and it may be necessary to examine the nerves.

I conclude from a study of this case: 1. That Head is probably correct in placing the umbilicus between the ninth and tenth thoracic sensory areas.

2. That the Babinski reflex may be absent in cases of lesion of the lumbar and sacral regions of the cord, though the clinical symptoms may indicate merely that the cord is compressed above the lumbar region. The absence of the Babinski reflex in such cases may possibly be a valuable sign of disorganization of the lumbar and sacral regions.

3. That while loss of the patellar reflexes may occur from transverse lesions of the cord above the lumbar region, the cause of this loss in a certain number of cases is to be found in lesions of the area through which the reflex arc passes.

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A CASE OF PRIMARY DEGENERATION OF THE PYRAMIDAL TRACTS.*

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Spastic spinal paralysis, lateral sclerosis, described separately by Charcot and Erb, has not an uniform pathological basis. Primary degeneration of the pyramidal tracts alone, *i.e.*, a degeneration confined to these tracts, and not resulting from a focal lesion, may occur, but certainly is very rare. The most recent paper on this subject with which I am familiar, is by Ida Democh[2], and she is able to refer only to the cases of Morgan and Dreschfeld[3], and Dejerine and Sottas[4]. She reports a case that is complicated. She speaks of Morgan and Dreschfeld's case as being the least complicated in the literature, and yet some of the cell-bodies of the anterior horns of the spinal cord were diseased in this case The examination of the tissues was made more than twenty years ago when the method of Nissl was not in vogue, and it is highly probable that could this method have been employed the nerve-cell bodies would have appeared more diseased than they did. The case seems to have been one of amyotrophic lateral sclerosis.

In Dejerine and Sottas' case the columns of Goll were not intact but the nerve cell-bodies of the anterior horns appeared to be normal, although the method of Nissl was not employed.

Ida Democh's case was complicated with neuritis from chronic alcoholic intoxication. The columns of Goll were degenerated in the cervical and upper thoracic regions. The nerve cell-bodies in the anterior horns of the spinal cord were not diminished in number, but apparently the Nissl method was not employed, so that we must remain in doubt whether these cell-bodies were perfectly normal or not. This omission is unfortunate, because in addition to the lateral sclerosis alcoholic neuritis probably existed, and there was therefore a double cause for cellular alteration in the spinal cord.

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*Read before the Philadelphia Neurological Society, March 25, 1902.

One of the most satisfactory cases yet reported is the case given in abstract recently by Strümpell[5]. This patient was 61 years old when first seen by Strümpell, and he was under his observation for almost fifteen years. The case was one of uncomplicated spastic spinal paralysis. The first signs of the disease began in 1866. The rigidity of the lower limbs developed gradually and became intense, and the tendon reflexes were much exaggerated. No fibrillary tremor and no trace of atrophy could be detected. The vesical and rectal functions were not affected. Sensation was normal until near death when some unimportant alteration of sensation was detected. The pyramidal tracts were degenerated, more in the lower thoracic and lumbar regions, and the degeneration did not extend above the pyramids. The columns of Goll were slightly degenerated in the cervical region. The nerve cell-bodies of the anterior horns were perfectly normal. It is presumable that they were examined by the method of Nissl, although the method of examination is not recorded in this abstract. The direct cerebellar tracts may have been slightly degenerated. Strümpell thinks that there can be no doubt that the spastic spinal paralysis from primary degeneration of, and confined to, the pyramidal tracts exists. The upper limbs are not affected in one form of this paralysis, and the disease may be hereditary. Another form is seen in more advanced life, and has a more rapid course, and all the limbs become spastic; finally, there may be slight atrophy of the muscles, so that this form cannot be sharply separated from amyotrophic lateral sclerosis. Two cases of the second type have been studied anatomically by Strümpell.

A third form occurs in childhood and may be hereditary. The pathology of this form has not been determined, except in so far as shown by Bischoff's[6] two cases in brothers, which are not altogether satisfactory. Bischoff found degeneration of the pyramidal tracts as high as the motor decussation, of the columns of Goll, of the direct cerebellar tracts and of the cell-bodies of the anterior horns of the cord and of the motor cortex. These cases cannot be regarded as uncomplicated either from a clinical or pathological viewpoint.

A few cases have been reported in which the primary degeneration of the pyramidal tracts was associated with degeneration of the direct cerebellar tracts, without alteration of the nerve cell-bodies.

My case reported in this paper, has resemblance to Strümpell's[7], published in 1894, in which degeneration of the cell-bodies of the anterior horns existed, although muscular atrophy was not detected during the life of the patient.

A. G., a woman fifty years of age, was admitted to the Philadelphia Hospital, Feb. 26, 1901, complaining of loss of power in the lower limbs, and difficulty of speech. She was at first under the care of Dr. F. Savary Pearce, but later came into my service. The clinical notes, obtained at the time of her admission, were made by Dr. Pearce and the resident physician, Dr. Geisler.

Family history: Her father, mother and one brother were dead from unknown causes.

Personal history: She was the mother of three children, and had had one miscarriage since the birth of her last child. Three years before admission, while coming home from work, she became dizzy, but managed to reach her home without falling. She had not been feeling well for some time. A physician was called and by the time he reached the patient her left upper limb was powerless and she had lost the power of speech. She did not lose consciousness. In a day speech returned, but she has never been able to speak distinctly since the attack. She was able to move her left upper limb within two or three days, and she returned to her work after about three weeks, having recovered except that her speech was still indistinct.

About a year before admission, weakness of the lower limbs was noticed, and this weakness gradually increased in intensity so that she walked very little. Her memory had deteriorated.

On admission she was able to walk with difficulty, and her gait was not distinctly spastic, and her steps were short. She swayed when standing erect, probably from weakness. Her speech was indistinct and bulbar in character.

She was a well-developed muscular woman. Her face was smooth and free from wrinkles below the forehead, but the forehead was wrinkled on both sides. When her mouth was opened it was drawn toward the right side. The naso-labial fold on the left side was not so distinct as on the right. The tongue was protruded straight, but the mouth was not widely opened. Both eyes could be closed. The irides reacted slowly to light and in accommodation. There was apparently no paralysis of the pterygoid, masseter and temporal muscles. There was no disturbance of deglutition.

The chest was well-developed and no atrophy was visible.

The left upper limb was moved freely but was weaker than the right, and the grip of the right hand was stronger than that of the left. There was no atrophy of the hands.

The lower limbs were moved freely, but were weak, and were not atrophied.

The reflexes were as follows:

	RIGHT	LEFT
Biceps-jerk	Much increased.	Increased.
Triceps-jerk	Much increased.	Increased.
Flexors at wrist	Much increased.	Increased.
Extensors	Much increased.	Increased.
Von Bechterew's	Absent.	Absent.
Epigastric	Absent.	Absent.
Knee-jerk	Much increased.	Increased.
Quadriceps-jerk	Much increased.	Increased.
Achilles-jerk	Present.	Present.
Plantar reflex	Increased	Increased.
Babinski's	Extension of great toe.	Slight extension of great toe.
Ankle-clonus	Absent.	Absent.
Patellar clonus	Absent.	Absent.

There were no disturbances of sensation, and stereognostic perception was normal.

She had been constipated and had noticed an increasing difficulty in retaining the urine for five months, but had not had absolute incontinence.

She had had dull headache over the whole of the head for one year, and occasionally had had pain in the left side of the face and in the back, but she had not had pains in the limbs.

On March 3, 1901, Dr. Charles A. Oliver examined her eyes and reported: "Left pupil is the larger. The irides are extremely sluggish to light, particularly the left one; quite prompt to accommodation and convergent efforts. Paresis of left external rectus muscle. Eyegrounds are healthy."

An urinary examination made March 1, 1901, gave the following results: "Lemon color, sp. gr. 1011, reaction acid, sediment white; microscopical examination: pus and epithelial cells; chemical analysis: albumin, small amount; no sugar."

Another examination made July 8, 1901, showed granular casts and epithelial cells, and a large amount of albumin.

On July 3, 1901, the following notes were made by me: The patient is in a stuporous condition, although she replies to questions and moves her limbs on command. She permits the flies to collect on her face, and even on the inner side of the lips or within the mouth, without attempting to brush them away. She can give her name, but is unable to give her age, or to say how long she has been in the hospital. Her speech is thick. She has incontinence of urine and feces. She is paretic in the lower limbs, though she can move all the muscles of these limbs. The lower limbs are not atrophied and are flaccid.

In testing sensation no dependence can be placed on her statements, but she recognizes the point of a pin and withdraws either lower limb when it is stuck with a pin.

The knee-jerk on the right side is diminished, and is less intense than that on the left, which is also impaired. The Achilles-jerk on the right side is present, but feeble; on the left side it cannot be distinctly obtained. The plantar reflex is exceedingly active on each side, and the Babinski reflex is pronounced on each side. [A few days later the Babinski reflex was absent on each side, and no movement of the toes was obtained by irritation of the sole of the foot. The loss of this reflex was probably a result of the increasing stupor.]

She moves the upper limbs freely, and these limbs are not distinctly paretic. There is no distinct atrophy of the upper limbs. When the upper limbs are stuck with a pin she shows signs of discomfort.

The pupils are unequal, the left being larger than the right. The movements of the eyeballs seem to be free in all directions. The irides contract feebly to light; there is very little contraction in convergence. She closes the eyelids firmly. Both upper lids droop so that the palpebral fissures are narrow.

The heart sounds are very loud, and the first sound at the apex beat is suggestive of a murmur, the murmur however is not transmitted into the axilla. The second pulmonic sound is somewhat accentuated.

The patient became progressively weaker, pulmonary and cardiac disturbance and fever developed, and she died July 10, 1901.

The pathological diagnosis made by Dr. W. F. Hendrickson, July 11, 1901, was: "Acute lobar pneumonia, chronic interstitial nephritis, hypertrophy and dilatation of heart, general arteriosclerosis, localized chronic pericarditis, chronic endocarditis, parenchymatous degeneration of myocardium, edema and congestion of lungs, early acute splenic tumor, parenchymatous degeneration of liver, chronic gastritis."

The brain and spinal cord were examined by me. Microscopical sections were made from the left paracentral lobule, the right cerebral peduncle, pons and lower parts of the central nervous system.

A slight recent hemorrhage was found within the cortex of the left paracentral lobule. The cell-bodies of this lobule could not be well studied by the thionin stain. No meningitis was found over this lobule, but the blood vessels of the pia at this part were slightly thickened.

The foot of the right cerebral peduncle was not degenerated either when studied by the Weigert hematoxylin or the Marchi stain. The right oculomotor nucleus contained many nerve cell-bodies and nerve fibers. A group of thickened blood vessels, surrounded by round-cell infiltration and the remains of an old hemorrhage, was found within the right cerebral peduncle near the oculomotor nuclei. No meningitis was found at the foot of the peduncle, and the blood vessels of the pia at this part were not much thickened.

The motor tracts within the pons were very slightly degenerated. The nucleus of each sixth nerve seemed to be normal. Very slight degeneration by the Marchi stain was found in the right pryamid, and none was found by this stain in the left pyramid. The cell-bodies of the nucleus of each twelfth nerve were shown to be deeply pigmented by the Marchi stain. The cell-bodies of these nuclei were numerous, but possibly not so numerous as in normal sections, and so far as could be determined by imperfect thionin staining they were not much diseased. The intramedullary portions of the twelfth nerves were normal. No meningitis was found over the medulla oblongata, and the vessels of the pia were not notably thickened. The anterior pyramids were slightly degenerated as shown by the Weigert hematoxylin stain, and the left pyramid was a little more degenerated than the right.

The degeneration of the pyramidal tracts in the spinal cord, as shown by the Marchi method, was very slight, but when the Weigert hematoxylin stain was employed the crossed pyramidal tracts in the lower cervical and lumbar regions were found distinctly but by no means completely degenerated, and the degeneration was therefore of long standing. It was equal on the two sides of the cord. The direct cerebellar tracts were normal The posterior columns were apparently intact. The direct pyramidal tract on the left side in the cervical region was slightly degenerated. The cell-bodies of the anterior horns in the lower cervical region were not so numerous as in normal sections, and some of these cell-bodies were diseased; *i.e.*, some were shrunken and had lost their chromophilic elements. The anterior roots of the lower cervical region appeared to be normal; except that some of the axones may have been slightly swollen.

In the lumbar region the cell-bodies of the anterior horns were not so numerous as in normal sections, and some of these cell-bodies were diseased in the same way as those of the cervical region. The anterior roots seemed to be normal.

Summary.—A woman fifty years of age developed suddenly weakness in her left upper limb with loss of speech. The power of speech was regained after a day or two, but never again was normal. The weakness almost entirely disappeared from the left upper limb after about three weeks. Two years after this attack she noticed that she was weak in her lower limbs, and the weakness gradually increased so that walking became difficult. The reflexes in all the extremities were exaggerated, and the Babinski reflex was obtained. The gait was not decidedly spastic. The right upper limb was not distinctly paretic, but the left was a little weak. No objective sensory disturbances were found, and no pains were felt in the limbs. Muscular atrophy was not observed, although the palsy of the lower limbs had existed more than a year. The reaction of the irides was sluggish. The left side of the face was slightly paretic, but the right side also probably was not normal.

Degeneration of the pyramidal tracts was found extending as high as the pons, but not above this. This degeneration was less intense in the anterior pyramids than in the spinal cord, and was equal on the two sides of the cord. The other tracts in the cord were normal. No meningitis was present.

Some of the small vessels of the cerebral pia were thickened, which in a person fifty years of age was not remarkable. The cell-bodies of the anterior horns of the spinal cord were in part diseased, and the nuclei of the hypoglossal nerves were probably not absolutely normal.

The attack of paralysis of the left upper limb probably with implication of the face, and with speech disturbances which developed two years before the other symptoms, cannot be satisfactorily explained by the findings. Amyotrophic lateral sclerosis does not usually begin in an apoplectiform manner. The degeneration of the pyramidal tracts extended equally high on the two sides, so that it is not probable that a focal lesion in the cerebrum was the cause of the degeneration in either tract; and no focal lesion could be found. A small hemorrhage in the brain may have occurred and caused the paralysis, but if so it did not lead to secondary degeneration. It seems not at all impossible that the sudden weakness of the left upper limb and of the left side of the face was the first sign of the amyotrophic lateral sclerosis, and that the weakness in the lower limbs developed so gradually that it caused little annoyance to the patient until a year or two later.

A case of amyotrophic lateral sclerosis with necropsy reported by Schlesinger[8] has a resemblance to my case. A man, seventy-two years old, received a severe mental shock and his speech became at once affected. Soon after this a temporary right-sided hemiparesis developed. The mouth was opened with difficulty and deglutition was affected. To the symptoms of bulbar palsy were added progressive spastic paresis, without distinct atrophy of the extremities, and with exaggeration of the tendon reflexes. An acute commencement or rapid progression of bulbar palsy, according to Schlesinger, should always suggest the possibility of amyotrophic lateral sclerosis.

The paralysis in my case beginning in the lower limbs and not implicating the upper limbs, except the persisting slight paresis in the left upper limb, dating from the apoplectic attack, is unusual in amyotrophic lateral sclerosis, but has been described as one of the signs of the spastic paralysis of Erb and Charcot from primary degeneration of the pyramidal tracts. The gait was not very spastic but it was weak and the tendon reflexes were exaggerated.

The absence of distinct muscular atrophy was one of the most interesting features of this case. The disease had existed more than a year, and therefore time for atrophy to develop had been given, and yet even in the lower limbs distinct atrophy was not observed. This is especially noteworthy, inasmuch as some of the cell-bodies of the anterior horns of the spinal cord were diseased. Had death been delayed atrophy might have been observed. It seems probable that the cellular changes developed later than the degeneration of the pyramidal tracts.

In the weakness of the lower limbs, the exaggerated reflexes without muscular atrophy, the gradual development of the paralysis—gradual because at the time of admission to the hospital the patient was still able to walk—the case presented the clinical picture of primary lateral sclerosis, and yet the microscopical examination showed that the cell-bodies of the anterior horns were implicated.

The slow reaction of the irides is not common in amyotrophic lateral sclerosis, but Schlesinger[8] has observed the Argyll-Robertson phenomenon in this disease. The slow reaction in my case may have been caused by anteriosclerosis.

Amyotrophic lateral sclerosis is usually regarded as a rare disease, and yet within the last three or four years I have studied the pathological material from five cases of this affection, but only two of these cases have been reported. I have seen quite a large number of clinical cases within this period, so that I am inclined to think that amyotrophic lateral sclerosis is not so rare as many physicians believe. In association with Dr. Dercum[9], and later in quite a long paper by myself[10], I have discussed the symptomatology and pathology of this disease, and it is hardly worth while to repeat what has been said. In only one of the five cases was I able to trace degeneration above the pons, and in that case the degeneration of the motor cortex was so intense that I believed that by the method of Marchi I might be able to define the extent of the cortical motor area, inasmuch as amyotrophic lateral sclerosis is essentially a disease of the motor system; an attempt which had never been made. This I was able to do, and I obtained a motor area corresponding quite closely to that described by von Monakow and others. The ascending frontal convolution was more degenerated than the ascending parietal, and this finding is especially interesting in connection with the recent results obtained by Schaffer[11] in his study of brains from cases of paretic dementia, and by Sherrington and Grünbaum[12] in their experiments on the brains of monkeys. These studies seem to show that the motor functions are represented in the ascending frontal convolution much more than in the ascending parietal convolution.

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Extracted from The American Journal of the Medical Sciences, July, 1902.

TWO CASES OF PARTIAL INTERNAL HYDROCEPHALUS FROM CLOSURE OF THE INTERVENTRICULAR PASSAGES:

WITH REMARKS ON BILATERAL CONTRACTURES CAUSED BY A UNILATERAL CEREBRAL LESION.[1]

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(From the William Pepper Laboratory of Clinical Medicine, Phoebe A. Hearst Foundation.)

Internal hydrocephalus is not a very uncommon finding at necropsy, but the cause of the increase in the amount of the cerebrospinal fluid within the ventricles has often eluded detection.

Two cases that have come under my observation, and have been studied by means of microscopical sections, have shown that the hydrocephalus was the result of closure of the interventricular passages, each case being one of partial dilatation of the ventricular cavity.

Partial internal hydrocephalus is more uncommon than is the form of the disease in which all the ventricles of the brain are implicated, and affords a better opportunity for determining the location of the primary lesion.

It is not necessary to study the different works on hydrocephalus very exhaustively to find that actually observed lesions are much rarer than theories explanatory of the causes of hydrocephalus. Oppenheim,[2] in the recent third edition of his text-book, remarks that we have very little positive knowledge regarding the pathogenesis of congenital hydrocephalus. It is assumed, he says, that an inflammatory condition of the ventricular ependyma, or an occlusion of the communicating passages between the ventricles, or between the ventricles and the subarachnoid space, is the cause. It is certain that this occlusion may be a cause of congenital hydrocephalus, but it is not known how often it occurs. Great importance is attributed to it by d'Astros, Boenninghaus and Dexler, and pathological findings showing that occlusion of these spaces may cause hydrocephalus are reported by Luschka, Monro, Neurath, and Bourneville and Noir.

Birch-Hirschfeld[3] and Ziegler[4] also say that the cause of internal congenital hydrocephalus is obscure. They refer to the various theories offered, and Ziegler states that in a few cases of unilateral hydrocephalus the foramen of Monro has been found closed, but he does not mention the names of those who reported these cases.

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[1] Read, in abstract, at the meeting of the American Neurological Association, June, 1902.

[2] Lehrbuch der Nervenkrankheiten, third German edition, p. 811.

[3] Lehrbuch der pathologischen Anatomie.

[4] Lehrbuch der speciellen path. Anatomie.

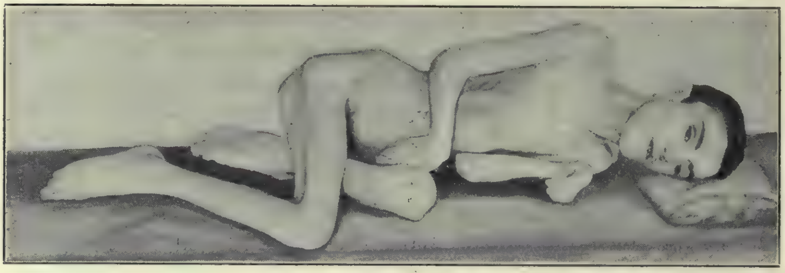
Dexler[1] has studied internal hydrocephalus in the horse, and believes that the condition in this animal is caused by occlusion of the aqueduct of Sylvius.

In the case of hydrocephalus in a child, published by Bourneville and Noir,[2] the aqueduct of Sylvius was completely obliterated and the fourth ventricle was only slightly dilated. A microscopical examination of the tissues apparently was not made.

Neurath's[3] case was one of occlusion of the foramen of Magendie.

A case similar to the second case reported by me in this paper has recently been placed on record by Touche.[4] The patient, a child, was in perfect health until the age of four years. At this period of its life it had repeated convulsions, and the head gradually increased in size, and both sides of the body became paralyzed. The lower limbs remained paralyzed, but some power was regained in the upper limbs. The patient lived to be twenty-nine years old. At the necropsy the fourth ventricle was found to be of normal size, but the aqueduct of Sylvius was completely obliterated, and the third and lateral ventricles were greatly dilated. A microscopical examination of the specimens is promised.

FIG. 1.



Unilateral internal hydrocephalus, causing bilateral contracture. Photograph taken after death. (Case 1.)

A case of unilateral hydrocephalus has recently been reported by W. C. White.[5] A woman, seventy-four years of age, had repeated hemiplegic attacks of comparatively short duration. The limbs on the paralyzed side were one centimetre less in size than those on the opposite side. The hemiplegic attacks had been diagnosed during life as the result of embolism. Intense unilateral internal hydrocephalus was found, the only causative lesion being obstruction in the left choroid plexus. The foramen of Monro was patent. White refers to a case of unilateral hydrocephalus following tapping for congenital hydrocephalus reported by Baskett.

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[1] Neurologisches Centralblatt, 1899, p. 977.

[2] Le Progrès Méd., July 14, 1900, p. 17.

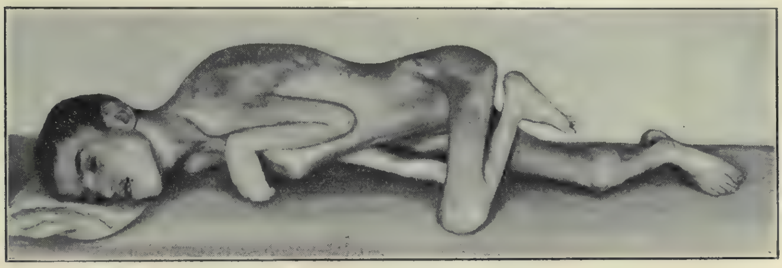
[3] Neurologisches Centralblatt, 1896, p. 87.

[4] Bulletins et Mémoires de la Soc. Méd. des Hôpitaux de Paris, 1902, No. 7, p. 141.

[5] W. C. White. American Journal of Insanity, vol. lviii., No. 3, p. 503.

The first case that I report in this paper was one of unilateral internal hydrocephalus. The right cerebral hemisphere was a mere sac, while the left was normal. Bilateral contracture from this unilateral cerebral lesion was very intense. Bilateral contracture from unilateral lesion is uncommon. The patient was an inmate of the New Jersey Training School for Feeble-minded Children. For the photographs (Figs. 1 and 2) I am indebted to the principal of the school, Mr. E. R. Johnstone.

FIG. 2.



Unilateral internal hydrocephalus, causing bilateral contracture. Photograph taken after death. (Case 1.)

Little is known of the history and clinical condition of E. R. At the time of death he was fourteen years and eight months old, and had been in the New Jersey Training School for Feeble-minded Children four and a half years. He came from the Hudson County Almshouse, and his parents were unknown. He was said to have had no convulsions during the time he was at the almshouse. He walked when he first came to the training school, but his gait was peculiar, and he went up and down stairs with difficulty. He was an idiot, and was never heard to speak. His ocular condition was unknown.

The following notes were made by Dr. Wilson, December, 1899. "The record of April 1, 1897, says: Ezra was quite sick last month, and was in bed for a number of days. Since then he has been more helpless than usual, and does not stand or walk.

"He has become more helpless the past year, so that he could not sit up straight. Since June, 1897, he has been bedfast."

Notes by Dr. Corson, August, 1897: "When E. R. was admitted he could walk and help himself quite a little, but since his last sickness he is entirely helpless; cannot walk, stand, or sit up, but lies down all the time. He had five spasms in the month of July."

The boy had several severe convulsions during the week ending December 9, 1899, and had been having them for at least two or three years. He died December 10, 1899. I never saw the boy during his life.

The necropsy was made by me Tuesday, December 12, 1899, at 10.30 A.M. I am indebted to Dr. C. W. Burr for the pathological material. My notes are as follows:

The left lower limb is firmly contractured at the knee and hip, so that the posterior part of the left leg is closely drawn to the posterior part of the left thigh. The left thigh is contractured on the pelvis to a right angle with the latter. The left leg can scarcely be extended at all at the knee, and the left thigh cannot be extended at the hip beyond a right angle with the pelvis, and when the left thigh is moved the pelvis is moved with it. The right leg lies at a right angle with the right thigh and cannot be extended beyond a right angle. The right thigh lies at an oblique angle with the pelvis, and the movement at the hip-joint is exceedingly limited. The left lower limb is much smaller in circumference than the right. The middle of the left leg measures 13 centimetres (5⅛ inches) in circumference; the middle of the right leg measures 15 centimetres (6 inches) in circumference; the middle of the left thigh measures 18 centimetres (7⅛ inches) in circumference; the middle of the right thigh measures 22.5 centimetres (8⅞ inches) in circumference; the right thigh from the great trochanter to the head of the fibula measures 28 centimetres (11 inches); the left thigh measures 28 centimetres (11 inches); the right leg from the head of the fibula to the external malleolus measures 28 centimetres (11 inches); the left, 28 centimetres (11 inches). The left foot is smaller than the right, and the fourth toe is almost the same size as the fifth toe on the left side.

The right arm from the greater tuberosity of the humerus to the external condyle measures 23 centimetres (9 inches); the left, 22 centimetres (8⅝ inches); the right forearm from the external condyle to the styloid process of the radius measures 18 centimetres (7⅛ inches); the left, 16.5 centimetres (6½ inches). The middle of the left forearm measures 10 centimetres (4 inches) in circumference; the middle of the right forearm, 10.5 centimetres (4⅛ inches) in circumference; the middle of the left arm, 11.5 centimetres (4½ inches) in circumference; the middle of the right arm, 15.5 centimetres (6½ inches) in circumference.

The right upper limb is fully extended, but the fingers show slight contracture. When the right hand is flexed on the forearm the fingers can be fully extended, but when the right hand is extended the fingers are flexed and cannot be extended—*i. e.*, the flexor tendons are shortened.

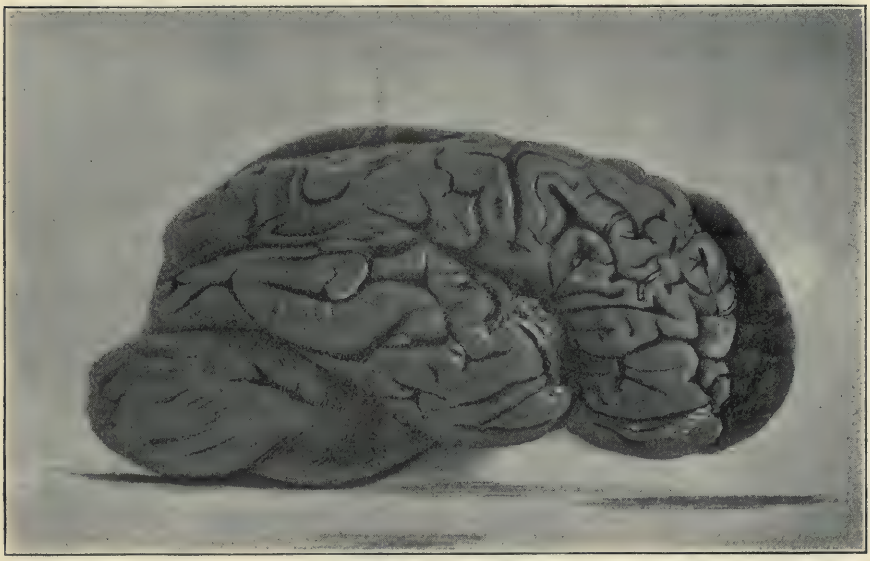
The ends of the fingers of the right hand are very blue. The left arm is firmly drawn to the side of the thorax, and can only be moved slightly. The left forearm is at an acute angle with the left arm, and cannot be extended at all. The fingers are mainly in extension, although there is a tendency to flexion.

The thorax is markedly pigeon-breasted, but other signs of rickets are not very evident.

The circumference of the head is 46.5 centimetres (18¼ inches). The distance from the glabella to the inion is 28 centimetres (11 inches). The lower part of the face is protruding. The forehead is narrow. The pupils are equal. The left corner of the mouth is slightly higher than the right, as though facial contracture were present on the left side.

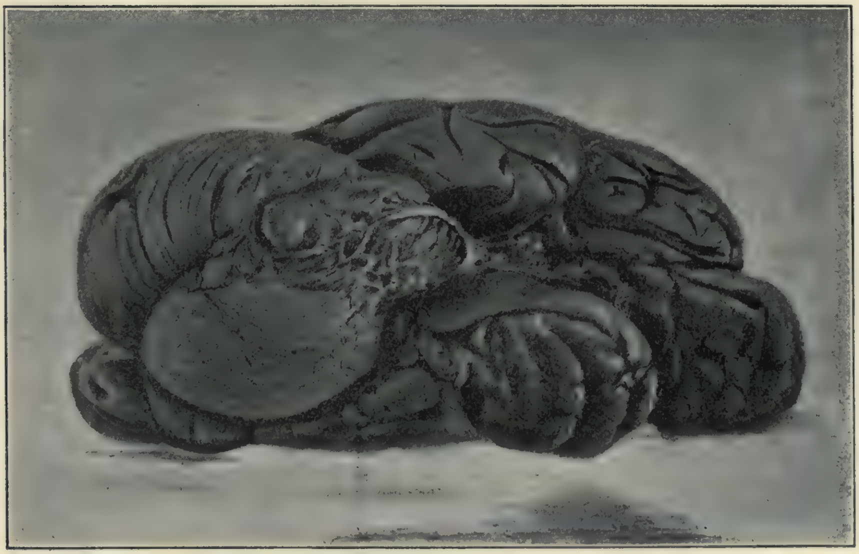
The skull is exceedingly thick, especially in the right frontal region,

FIG. 3.



Brain from a case of internal hydrocephalus of the right cerebral hemisphere. The right cerebral hemisphere was much smaller than the left, and was merely a thin-walled sac. (Case 1.)

FIG. 4.



Basal aspect of brain from a case of internal hydrocephalus of the right cerebral hemisphere. The left lateral lobe of the cerebellum is much smaller than the right. (Case 1.)

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where it measures 1.2 centimetres (½ inch). Before the dura is cut the frontal lobe on the right side is much less prominent than that on the left side. The brain is not very œdematous. The right cerebral hemisphere measures 15 centimetres (6 inches); the left, 16.5 centimetres (6½ inches). The resistance to the finger on palpation is much less over the frontal area of the right side than over the corresponding area of the left side, while the brain is within the cranium. The entire right cerebral hemisphere forms the wall of a cyst. (Figs. 3 and 4). The weight of the brain is 26.5 ounces. The cerebro-spinal fluid on the exterior of the brain is not abnormal in amount. There is a distinct kyphosis involving the entire vertebral column.

The pericardial fluid is small in amount. The heart weighs 43 ounces. A chicken-fat clot is found in the right ventricle. The tricuspid valve is normal. The wall of the right ventricle is thin. The pulmonary valves are normal. A chicken-fat clot is found in the left ventricle. The aortic valves are normal.

No excess of fluid and no adhesions are found in the pleural cavities. The right lung weighs 4 ounces and is crepitant throughout. A piece of this lung placed in water floats. The left lung is crepitant and shows hypostatic congestion. Weight of left lung is 7.5 ounces.

The liver extends to within two fingers' breadth of the last rib. The liver on its under surface and the adjoining structures are deeply stained with bile. Numerous apparently fatty areas are found in the liver. The weight of the liver is 14.5 ounces.

The right kidney contains numerous cysts and also a pus cavity. One of the cavities is filled with a cheesy granular mass. The right kidney weighs 2.5 ounces.

The right suprarenal body appears to be tuberculous.

The left kidney is much larger than the right. The capsule strips easily on each kidney, and no cysts are found in the left kidney. The weight of the left kidney is 4.5 ounces. The left suprarenal body is normal.

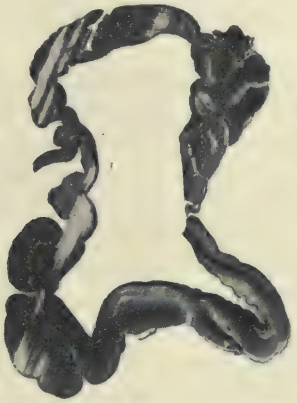
The spleen is small and apparently normal in appearance. It weighs 1.5 ounces.

The wall of the bladder is not thickened and is filled with purulent urine.

A series of microscopical sections of the basal ganglia of the right cerebral hemisphere and sections of the pons and parts below were made. The structures of this cerebral hemisphere were found much atrophied. The choroid plexus was much thickened at the right foramen of Monro, and contained numerous masses of cells with round nuclei. A nodule, in continuity with the external wall of the foramen, projected into the foramen. This nodule at one part was bordered by cells with round nuclei several layers deep, and these were evidently derived from the ependymal lining. Similar layers of cells, derived from the ventricular ependyma, bordered the external wall of the foramen and the adjoining parts. The nodule was composed of tissue like that of the brain substance, although its structure resembled also fibrous connective tissue. The inner wall of the right foramen of Monro contained a small nodule in which were many cells with round nuclei, and the nodule projected slightly into the foramen. The alteration of the walls of the left foramen of Monro was slight. The pyramidal tract on the right side of the pons was much smaller than that on the left, but the bundles of fibres present in the pyramidal tract on the right side were very slightly degenerated, as shown by the Weigert hæmatoxylin stain. The right anterior pyramid was only slightly degenerated, but it was smaller than the left. The left crossed pyramidal tract in the spinal cord was slightly degenerated. The right crossed pyramidal tract in the spinal cord appeared a little less deeply stained by the Weigert hæmatoxylin method than the surrounding parts of the antero-lateral column. The nerve cell bodies in the anterior horns of the cervical and lumbar regions were equally numerous on the two sides and apparently normal in form and number.

SUMMARY. The patient, a boy, was fourteen years and eight months old at the time of death. Little is known of his history, as he had come from an almshouse. Four years before death he had been able to walk with difficulty and to ascend stairs, but he gradually lost this power and became bedridden. Contractures were very pronounced in the left limbs, and also, but to a less extent, in the right lower limb and fingers of the right hand. The right cerebral ventricle was intensely dilated, so that the ventricular wall in some places was very thin, the occipital lobe at parts being only ⅛ inch thick. (Fig. 5.) The right internal hydrocephalus was the result of partial closure of the right foramen of Monro from inflammatory changes about this foramen, and the condition must have been congenital or have developed early in life, as shown especially by the arrest of development of the left upper limb. The cause of these inflammatory changes and proliferation of neuroglia at the foramen of Monro is unknown, but it may possibly have been the result of tuberculosis, as a condition of some of the viscera suggestive of tuberculosis was found. Anglade[1] has described neurogliar pro-

FIG. 5.



Photograph of a microscopical frontal section of the right occipital lobe (natural size), showing great distention of the posterior horn of the lateral ventricle. The walls of the posterior horn have become approximated during the process of hardening. (Case 1.)

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[1] Revue Neurologique, February 15, 1902, p. 113.

liferation in the walls of the ventricles, occurring in cases of general tuberculosis, and produced by the toxin of the tubercle bacillus. This neurogliar proliferation resembles very closely that found in cases of cerebral syphilis or paretic dementia. These ependymal nodules do not contain bacilli. Probably there are many causes for neurogliar proliferation of the ventricles.

Notwithstanding the very intense muscular atrophy in this case the cell-bodies of the anterior horns of the lumbar and cervical regions appeared to be normal. This finding is important and shows the difficulty of explaining muscular atrophy in hemiplegia as a result of tertiary degeneration—*i. e.*, a degeneration of the cell-bodies of the anterior horns of the spinal cord resulting from the degeneration of the pyramidal tract.

Bilateral contracture from unilateral cerebral lesion is not mentioned in most of the text-books, and is of rare occurrence, especially in the intensity observed in my case. It seems to be almost unknown outside of the French school.

Brissaud,[1] in his monograph on hemiplegic contracture, published in 1880, refers to an observation of Poumeau, reported by Hallopeau,[2] in which a hemiplegic became paralyzed on the " sound " side. Hallopeau believed that the extension of the paralysis was the result of extension of secondary myelitis. In this monograph Brissaud stated that there were many hemiplegic women in the Salpêtrière who after a certain number of years had become paralyzed, and the paraplegia was complicated by contracture to such a degree that the thighs were drawn against the abdomen and the chin touched the knees, and extension of the lower limbs had become impossible. He gives two illustrations of this bilateral paralysis, in each of which one lower limb was considerably more contractured than the other. Brissaud thought that these cases were not very rare, but as regards the pathology he could merely say that some day we should learn the cause of this bilateral paralysis.

Paul Dignat,[3] writing in 1883, remarked that secondary contracture is not always limited to the hemiplegic side. In the great majority of cases, he says, it is found only in the limbs of the paralyzed side, but in some cases it develops in both lower limbs. Cases of this character are relatively rare, and in this statement he seems to disagree with Brissaud, who apparently regarded them as more common than did Dignat. The latter refers to Hallopeau's case, in which all four limbs were contractured, the hemiplegia of the left side having existed since childhood. A cyst was found within the right parietal lobe. He refers to two similar cases with necropsy, published by Pitres,[1] and to a case published by Féré[2] without necropsy, and reports two cases himself without necropsy.

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[1] " Recherches anatomo-path. et phys. sur la contracture permanente des hémiplégiques," par E. Brissaud, Paris, 1880, p. 76.

[2] Arch. gén. de Méd., 1871, p. 449.

[3] Le Progrès Médical, 1883, vol. ii. p. 802.

In one of his cases the patient was eighty-seven years of age, and the hemiplegia had existed for a year, and this case shows that bilateral contracture is not confined to those cases in which the hemiplegia develops in childhood.

Marie[3] refers to the contracture of both lower limbs occurring in hemiplegia, but he gives no examples of this except in the picture he borrows from Brissaud's monograph published in 1880.

One of the most recent works on nervous diseases is by Dejerine.[4] He mentions Hallopeau, Brissaud, Pitres, and Dignat as having observed contracture of the " sound " side in hemiplegia, but he gives no references to recent observations on this subject.

Brissaud[5] asserts that contracture is never found in the upper limb on the " sound " side, and my case alone would show that this statement is erroneous.

The explanation for the bilateral contracture in hemiplegia is to be found in the innervation of both sides of the body from each side of the brain. There can be no doubt that each cerebral hemisphere innervates both sides of the body, but the fibres innervating the so-called sound side are fewer in number, and therefore the contracture on this side, when it occurs, is less intense than on the more paralyzed side, and this was the condition in my case.

Von Monakow[6] refers to the remarkable fact that the intensity of contracture need not be proportional to the number of degenerated pyramidal fibres; in other words, that sometimes partial interruption of the pyramidal tract may cause a more intense contracture than complete destruction of this tract. The contracture in partial destruction of the tract is the result of irritation of the remaining pyramidal fibres and of the partial loss of inhibition through degeneration of some of the fibres. Von Monakow accepts the teaching of Exner and Sternberg, that excito-motor (" bahnende ") fibres exist in the central nervous system as well as depresso-motor fibres, and by irritation of the former the muscular tonus may be exaggerated and contracture result. The excito-motor fibres are contained in the pyramidal tract, but are not confined to this tract.

The bilateral contracture in my case possibly may be explained by a partial loss of cerebral inhibition, as a result of which the muscular tonus was exaggerated, this exaggeration being also occasioned in part by irritation of the excito-motor fibres. The early age at which the hydrocephalus developed may have aided in the increase of muscular tonicity. The pyramidal tract from the right cerebral hemisphere was only slightly degenerated, and the case is proof, therefore, of the correctness of von Monakow's statement, that partial interruption of the motor tract may cause a more intense contracture than complete destruction of this tract.

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[1] Soc. de Biol., 1880, and Soc. Anat., 1881.

[2] Archives de Neurologie, 1882, No. 10, p. 61.

[3] Vorlesungen über die Krankheiten des Rückenmarkes (translated from the French), pp. 25, 27.

[4] Sémiologie du Système nerveux, p. 486.

[5] Traité de Médecine, p. 41.

[6] Gehirnpathologie, p. 302.

The second case that I report was in the service of Dr. C. K. Mills, at the Philadelphia Hospital, and I am indebted to him for the clinical notes and the pathological material. I saw the patient with Dr. Mills many times. The internal hydrocephalus was the result of closure of the aqueduct of Sylvius by proliferation of the neuroglia, and caused the symptoms of cerebellar tumor. The ventricles, except the fourth, were much dilated, the fourth being of normal size.

H. C. was admitted to the Philadelphia Hospital on October 28, 1901. He was a well-developed youth, aged nineteen years. He said that he had had slight headache once or twice a week since he was a child, and each attack of headache was associated with vomiting. About July, 1901, the headaches became more intense, although they did not increase in frequency. The vomiting continued, and he now began to have difficulty in walking. He felt dizzy at times, and staggered like a drunken man. This disturbance of gait came on suddenly, and had persisted. He did not have pain in the eyes, and had always slept well. While lying on his back he occasionally felt dizzy, and the dizziness was relieved by turning on his side.

He had been a constant cigarette smoker, using as many as thirty to fifty cigarettes in a day. He used coffee and tea to excess, and had been a moderate drinker of alcohol. He denied all venereal disease.

An examination made October 30, 1901, gave the following results:

The eyes show some exophthalmos, which patient asserts has always been present. He has always been myopic. The irides react to light and in accommodation. The tongue is protruded straight, and shows slight tremors. No palsy of the muscles of the arms is detected. The grip of the hands is fair. Both knee-jerks are exaggerated, but no ankle clonus is obtained. Slight patellar clonus is present on each side. The muscle-jerks are increased. The Babinski reflex is absent on each side. The station with feet apart is good, but with feet together is poor, and sway is not increased by closure of the eyelids. The gait is unsteady, and at times he has to catch hold of the bed to keep from falling. Sensation to touch and pain seems normal.

Notes by Dr. de Schweinitz are as follows: "The patient has always been myopic. The myopia is between 3 and 4 diopters. In each eye there is well-marked beginning optic neuritis. Arteries about normal in size. Veins are tortuous. On right side a few small hemorrhages down from disk are found. The neuritis is about even on the two sides. Reactions of irides are normal. The form fields are normal. Rotation of eyes is normal. The patient has had double vision."

January 2, 1902. The patient to-night had a slight tremor of the muscles of the arms and face, lasting a few seconds; this was followed by unconsciousness, stertorous breathing, and irregular and rapid pulse. He became cyanotic. The saliva flowed from the mouth, and slight nystagmus of both eyes, lasting about five minutes, occurred during the attack. The pupils were contracted. The pulse at the beginning of the attack was of good tension, but later became very rapid and weak, and stopped about four minutes after cessation of breathing. The pupils became dilated as the pulse became rapid.

The patient died at 7.25 P.M. January 2, 1902. The necropsy was made by Dr. F. J. Kalteyer, January 3, 1902.

Pathological Diagnosis. Œdema and congestion of the lungs; internal hydrocephalus.

On removing the skullcap, which was extremely thin, the brain substance and its membranes bulged outward. On the internal surface of the skullcap the moulding of the convolutions of the brain could be distinctly made out. The third and lateral ventricles of the brain are distended with clear fluid having a specific gravity of 1010. The aqueduct of Sylvius is not patulous.

SUMMARY. The patient, a boy, aged nineteen years at the time of death, had had some headache once or twice a week, with vomiting, since childhood; but about six months before death the headaches became severe, and cerebellar gait was observed. Dizziness was also experienced, especially when the patient laid on his back. This dizziness was probably the result of pressure of the distended cerebral ventricles on the cerebellum. Slight exophthalmos was observed. Distinct optic neuritis was present in each eye. The knee-jerks were exaggerated. Death occurred suddenly.

The skull was very thin—hardly thicker than a sheet of paper at the sides of the calvarium. The cerebral ventricles were much distended, but the fourth ventricle was of normal size. The aqueduct of Sylvius was entirely occluded when examined by the naked eye, but in microscopical sections (Fig. 6) a very small opening was found, which may have been absent during life. It is questionable whether any fluid passed through this opening during life. Small groups of ependymal cells were seen in several places, and these had evidently been separated from the ependymal lining by the proliferation of the neuroglia.

Oppenheim[1] has described a case of myasthenia gravis pseudoparalytica in which he found bridging over of the aqueduct of Sylvius, and in some sections a third canal. Such anomalies of this region he believed had never previously been described. The occlusion in the case H. C., reported by me, must be of the same character as the partial occlusion in Oppenheim's case, and was probably congenital or acquired early, on account of the history of headache and vomiting dating from childhood. The occlusion must have become complete about six months before the patient's death, when the symptoms became much more intense than they had been previously. The closure of the aqueduct of Sylvius resembles in the changes of tissue produced by it the condition often seen in the region of the central canal of the spinal cord.

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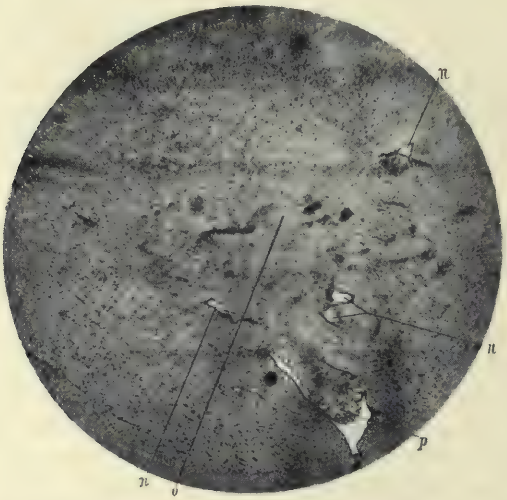
[1] Monatsschrift für Psychiatrie und Neurologie, March, 1900, p. 177.

The symptoms were exceedingly suggestive of cerebellar tumor, and in every case where a tumor of this portion of the brain is suspected the possibility of internal hydrocephalus should be borne in mind.

FIG. 6.



Occlusion of the aqueduct of Sylvius, causing internal hydrocephalus of the third and lateral ventricles. The fourth ventricle was not distended. *n*, *n*, *n*. Small masses of ependymal cells from the lining of the aqueduct, cut off by proliferation of the neuroglia. Other similar masses are not included in the photograph. *p*. Lower part of the aqueduct of Sylvius, almost entirely closed by the proliferated neuroglia. *o*. Area where the aqueduct formerly existed. (Case 2.)

This is by no means the first case in which the symptoms of brain tumor were caused by internal hydrocephalus. Byrom Bramwell,[1] some years ago, reported cases in which the characteristic symptoms of cerebellar tumor were present; but a distention of the ventricles, apparently the result of closure of the foramen of Magendie from localized meningitis, was found.

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[1] Brain, Spring, 1899, vol. xxii. p. 66.

6

CASE OF EXTERNAL SPINAL PACHYMENINGITIS, IMPLICATING THE ENTIRE VENTRAL SURFACE OF THE SPINAL DURA.

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From the William Pepper Laboratory of Clinical Medicine; Phœbe A. Hearst Foundation.

External spinal pachymeningitis, except the tuberculous variety of limited extent, is uncommon, and, so far as we know, no case of external spinal pachymeningitis is on record in which the entire ventral surface of the dura, from the foramen magnum to the caudal end of the dural sheath, was adherent to the bodies of the vertebræ by fibrous proliferations, and the rest of the spinal dura was normal. Such a case forms the subject of this paper.

A man, white, 42 years old, piano-tuner by occupation, was admitted to the Philadelphia Hospital, February 17, 1896. No family history of importance was obtained except that two brothers and three sisters died in childhood. The patient had been blind since he was three months old. During his early life he had scarlet fever, pneumonia, typhoid fever, and rheumatism. He drank moderately, and denied venereal disease.

In June, 1895, he, for the first time, had a feeling of numbness in the right great toe. This numbness, after gradually spreading to the knee, attacked the other foot and leg in the same way. He had no pain, but the numb limbs felt as if asleep. Previous to the numbness he had had, for a time not fixed, some swelling and tenderness in the legs, and an aching pain in the lumbar region. He could walk until November, 1895, but his knees became bent (probably from spasticity), and he felt as if walking on springs. He began to have nocturnal incontinence of urine in July, 1895.

On February 21, 1896, a few days after admission, the record was made of exaggerated reflexes in the lower extremities, with a tendency towards a spastic condition. Ankle clonus was marked in both feet. It is to be inferred that the condition noted as having developed between July and November, 1895, was still present, namely, numbness in the lower extremities, inability to stand and walk, and incontinence of urine. His heart and vessels were described as normal, lung expansion was good, and respiratory murmur was normal. His bowels were constipated. On October 12, 1898, a note was made that sensation was intact, that the knee-jerks were plus when the muscles were relaxed, and that ankle clonus was not present, possibly on account of rigidity. Ward notes made on November 29, 1900, stated that the legs became rigid on effort; the patient could extend his lower limbs and stand, but could not walk; the knee-jerks were excessively exaggerated, and the irritation, in taking this reflex, provoked spasms of the legs in extension. Both legs also became firmly adducted; the feet were spastic at the ankles; no ankle clonus could be elicited; the Babinski reflex was typical and decided on both sides; sensation was everywhere well preserved; the legs appeared to be hypersensitive.

On April 17, 1901, it was noted that his right hand had been cyanotic and painful for some time. Signs of gangrene began to appear on two fingers of the hand. The patient was transferred from the nervous wards to the surgical wards for treatment. As the gangrene was evidently spreading, and as the patient suffered excruciating pain, amputation of the right hand was performed April 18, 1901. So far as the operation was concerned the patient in all respects did well. On May 9, 1901, he complained of severe pain in the left side, and auscultation revealed some suggestion of a friction sound. The temperature rose, and pulse and respiration increased. On the 10th dulness over the left lobe was observed, and breathing sounds were harsh. His active lung symptoms gradually subsided, and he was retransferred to the nervous wards. On June 22, 1901, he again complained of pain in the left side. On examination a fairly superficial friction rub was heard in the mid-axillary line on the left side, from about the fifth to the seventh rib. At the angle of the left scapula was an area in which expiration was shortened and harsh. The whole left base was dull and breathing sounds and expansion were much decreased; fremitus was not markedly altered. The patient's pulmonary condition again improved, and he remained in fair health until December. He was troubled from time to time with dyspnœa, and in October had an attack of copious hæmoptysis. On December 7, 1901, he was attacked with severe dyspnœa. Breathing was laboured and frequent, and speaking was difficult. Expansion was limited on both sides. He grew rapidly worse, and died on December 8, with œdema of both lungs. The symptoms referable to the nervous system remained practically the same during the last year or two of the man's life. He was frequently seen by one of us (Dr. Mills) during his term of service. The patient's condition from the notes already given and from recollection can be summarized as follows: He was paralysed in both lower extremities, and these were the seat of spasticity and marked contractures; all the deep and superficial reflexes in the lower extremities were much exaggerated, and he suffered from incontinence of urine; objective sensation was everywhere intact as late as November 29, 1900.

The necropsy was made December 8, 1901. It revealed many interesting pathological conditions in various parts of the body which, with the exception of the condition of the spinal dura and spinal cord, need only be briefly summarized here as follows: Thrombosis of the right pulmonary artery, cardiac dilatation, miliary tuberculosis and œdema of the lungs, parenchymatous nephritis and arteriosclerosis.

The external surface of the spinal dura on the ventral aspect was firmly adherent to the bodies of the vertebræ throughout the spinal canal. The dorsal aspect of the dura presented nothing abnormal, a single transection of the cord made between the tenth and the eleventh thoracic roots showed a gelatinous appearance to the naked eye in the crossed pyramidal tracts.

Microscopical examination reveals the following conditions:—

Sections from the right and left paracentral lobules appear to be normal, as do also sections from the medulla, except that the blood-vessels are distended.

Most of the nerve-cell bodies of the lower cervical region are well developed, although some appear atrophied, and here and there a few nerve-cell bodies in which the nucleus is displaced are found. Some small hæmorrhages of recent date are seen within the sections. The columns of Goll in the cervical region are much degenerated, and the degeneration is such as results from a lesion lower in the spinal cord. The ventral and dorsal roots appear to be normal. The direct cerebellar tract and the tract of Gowers on each side are degenerated. The crossed pyramidal tracts contain a slight excess of neuroglia, but by Weigert's hæmatoxylin stain do not appear degenerated. No signs of leptomeningitis are detected.

In the mid-thoracic region the degeneration is very intense, especially in the peripheral portions of the cord. Only the nerve-fibres near the central gray matter are intact. The anterior and posterior roots do not stain well, partly on account of the method of hardening, and it is difficult to decide concerning the condition of these roots. There is no evidence of leptomeningitis.

In the lumbar region the nerve-cell bodies seem to be normal. The crossed pyramidal tracts are degenerated, and the degeneration extends forward at the periphery of the cord, beyond the usual area of these tracts. The posterior columns are also partially degenerated. The condition of the anterior and posterior roots cannot be positively determined, as the roots do not stain well.

The dura, in its ventral portion, is composed of the

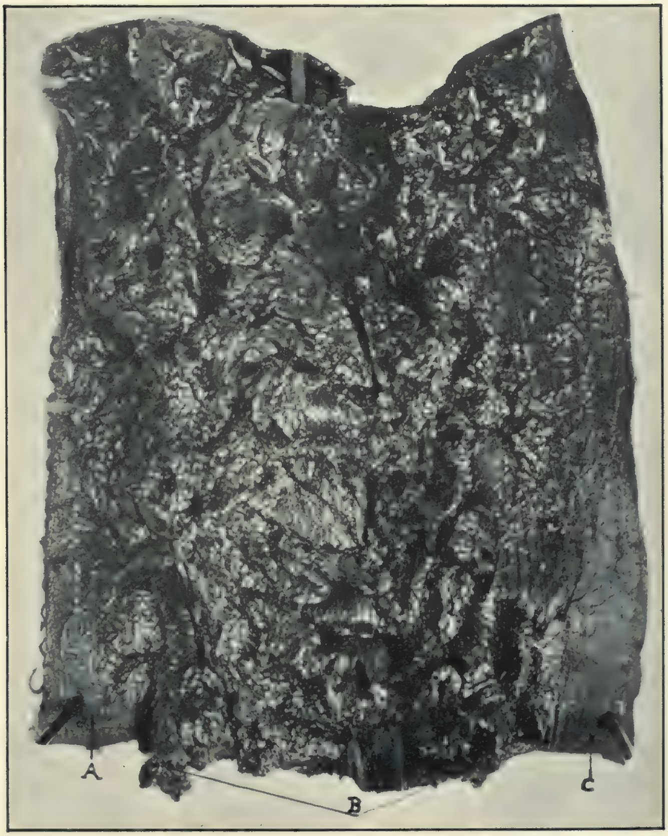

FIG. 1.

Photograph of the external surface of a part of the spinal dura.

The dura has been cut through in the dorsal portion. *A.C.* Dorsal portion of dura. *B.* Ventral portion of dura showing proliferation.

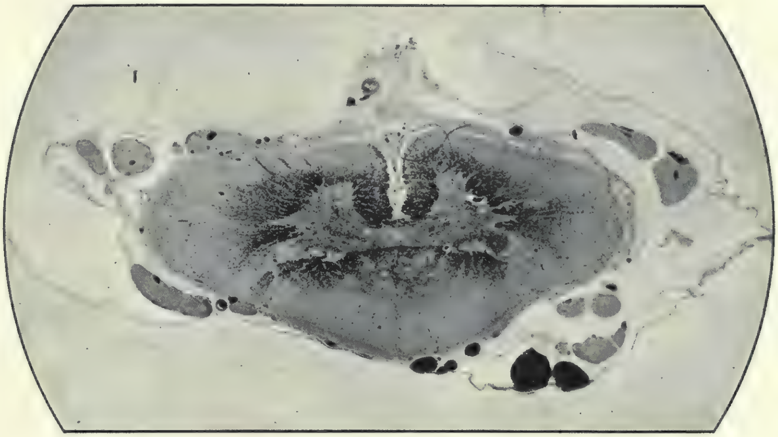

Fig. 2.

Photograph of a section from the mid-thoracic region.

The degeneration is intense in the peripheral portions of the cord.

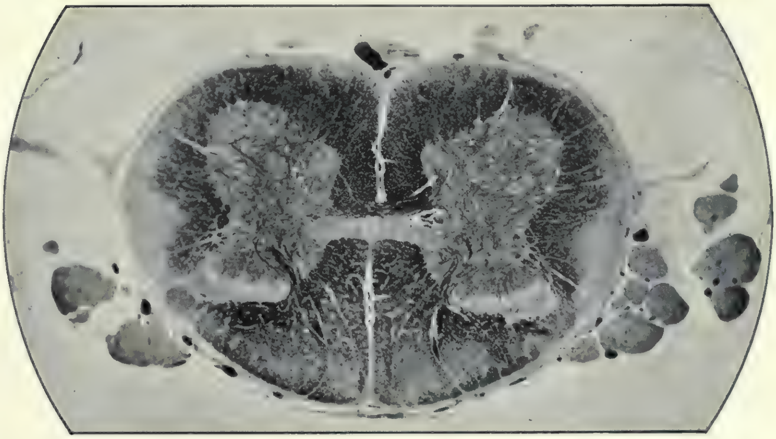

Fig. 3.

Photograph of a section from the lumbar region.

The crossed pyramidal tracts are degenerated, and the degeneration extends forward beyond the area of these tracts. The posterior columns are also partially degenerated.

fibrous tissue commonly found in this sheath, and the proliferations on the outer part of the dura are composed chiefly of the same fibrous tissue. At one place a small collection of cells with round nuclei, separated into groups by bands of fibrous tissue, is found, but collections of these cells with round nuclei are rare in the proliferations from the dura, and there is little evidence of acute inflammation. At some places what appears to be metastatic bone formation is found in the proliferations on the dura.

One of the ulnar nerves contains much excess of connective tissue between the nerve-bundles, and some of the nerve-bundles are partially degenerated. One of the musculospiral, one of the median, and one of the plantar nerves are in a similar condition.

A piece of muscle from the sole of the foot appears considerably atrophied, and numerous round nuclei are found in places between the muscular fibres, so that in these places myositis existed.

The eyeballs were examined by Dr. E. A. Shumway, whose report is as follows: "The smaller eye shows phthisis bulbi, with extensive bone formation in the interior of the eye, in the exudate on the choroid; nerve atrophic. The larger eye shows thick leucoma of cornea, staphyloma beginning; cornea entirely cicatricial; iris and ciliary bodies atrophied to a high degree; iris adherent to cornea throughout; organised tissue anteriorily due to old choroiditis; retina and choroid show chronic inflammation, with secondary pigmentation of the retina; optic nerve head deeply excavated, entirely atrophic."

Chronic external pachymeningitis of the cerebral dura is so rare that Alexis Thomson,[1] in 1894, said he had not been able to find the record of any specimen but that of the two which had come under his own observation. Lannelongue he mentions as having met with the condition while performing craniectomy in a case. One of Thomson's cases was in a child aged five years, who had died of abdominal tuberculosis. There was no sign or history of rickets or syphilis. The dura was firmly adherent to the calvarium, and on being forcibly torn from the bone presented on its outer surface a uniform layer of red sprouting granulations or villous processes. The inner table of the skull presented an infinite number of grooves and pits in which the granulations were embedded. The lesion was confined to the outer aspect of the dura in the region of the parietal eminences, and was perfectly symmetrical on the two sides, the cerebral surface of the dura being normal. Each process on the outer surface of the dura was made up of one or more capillary loops, surrounded by numbers of cells, the majority of which were leucocytes. Among these were a few scattered spindle-shaped corpuscles, and here and there clumps of red blood corpuscles. The cells and vessels were feebly supported by a very delicate recticulum of fibrin.

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[1] Alexis Thomson, *The Journal of Pathology and Bacteriology*, vol. ii., 1894.

The second specimen was found by Thomson in a museum.

Thomson believed that the characteristic features of the pathological process in these cases depended upon a reversal of the normal function of the dura, regarded in its capacity as an internal periosteum of the skull. Bone formation was replaced by the projection of vascular loops from the dura against the bone, leading to progressive softening of the latter, and the process was exactly like the method of absorption met with in inflammation (periostitis and osteomyelitis). Thomson says it was noteworthy that while the external surface of the dura was thickly studded with vascular granulations, there was scarcely any evidence of increased vascularity or of inflammatory changes in the substance of the dura. He regards the process as an aberration of development rather than as an inflammation. It caused no symptoms and showed no evidence of its existence during life.

External spinal pachymeningitis of non-tuberculous nature of limited extent has been occasionally observed. Stoubell's,[1] for example, reports a case of syphilitic external spinal pachymeningitis. A woman, aged 86, during one night became paraplegic in both lower limbs, and was anæsthetic as high as the umbilicus. The patellar reflexes were absent, and there was no ankle clonus. Death occurred two and a half weeks later from pneumonia. At the necropsy the thoracic vertebræ from the third to the sixth were found diseased, and the meninges in this region were thickened. A microscopical examination showed that the process was neither tuberculous nor carcinomatous. The meningeal growth had its origin from the outer surface of the dura, and was anteriorly united with the periosteum of the vertebral canal. It consisted of small-cell granulation tissue. The process was believed to be syphilitic. Stoubell remarks that syphilitic external pachymeningitis (peri-pachymeningitis) is extremely rare, and refers to cases reported by Virchow and Heubner.

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[1] STOUBELL, *Neurologisches Centralblatt*, 1898, p. 1, 120.

In the case described in this contribution, no disease of the vertebræ, to explain the adherence of the spinal dura to the bodies of the vertebræ, could be found at the necropsy, although no vertebral bodies were removed, and yet this adherence was so great that a knife was constantly employed to cut through the proliferation during the removal of the spinal cord and dura, and these proliferations consisted of dense fibrous tissue.

The degeneration of the posterior columns was probably caused in part by the degeneration of the posterior roots which were doubtless compressed by the abnormal fibrous tissue on the outer surface of the dura. Internal pachymeningitis or leptomeningitis did not exist anywhere. The intense degeneration of the thoracic region, especially of the mid-thoracic region, is difficult to explain. The spinal cord in the mid-thoracic region was very small, and the peripheral portions were entirely degenerated. The vertebral canal in the thoracic region is smaller than in the cervical or lumbar region, and if there were any œdema of the spinal cord, or any increase in the amount of the cerebro-spinal fluid, the effect of this pressure on a spinal cord firmly adherent by its dura to the bodies of the vertebræ might be most distinct in the thoracic region. The changes of the spinal cord in this region were such as might be produced by interference with the circulation and by pressure, and yet the nature of this pressure is not very evident, as the adhesions alone were hardly sufficient. The degeneration of the white columns of the cervical region was secondary to that of the thoracic region, as was also in part that of the lumbar region.

The degeneration of the peripheral nerves was probably caused by the involvement of the nerve-fibres, in passing through the thickened dura.

We cannot determine the nature of this external spinal pachymeningitis. There was very little evidence of acute inflammation, and the tissue forming the proliferations was chiefly of a fibrous character, and resembled closely that of the dura. It is possible that the process was syphilitic; but, if so, it was of a character very unlike that usually found in syphilitic lesions. Syphilis, when it occurs within the vertebral canal, usually causes a meningomyelitis, but there was not the slightest evidence of such a process in this case. The characteristic lesions of tuberculosis were not found within the vertebral canal. The external spinal pachymeningitis probably existed some time before it caused symptoms.

Such adhesions as existed in this case might have caused rigidity of the spinal column, but that does not appear to have been present. It seems remarkable that objective sensation was everywhere intact as late as November 29, 1900. It is possible that at that date very careful examination might have revealed some slight diminution in sensation, especially of the thorax or abdomen; it is also possible that the degeneration of the thoracic region of the spinal cord increased greatly during the last year of the patient's life, during which time no observation concerning sensation was recorded.

THE DIVISION OF THE SENSORY ROOT OF THE TRIGEMINUS FOR THE RELIEF OF TIC DOULOUREUX: AN EXPERIMENTAL, PATHOLOGICAL AND CLINICAL STUDY, WITH A PRELIMINARY REPORT OF ONE SURGICALLY SUCCESSFUL CASE.

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PART I.

BY WILLIAM G. SPILLER, M.D.

In a paper published in the November, 1898, number of the *American Journal of the Medical Sciences,* p. 532, I made use of these words: "If it could be shown that the sensory root of the Gasserian ganglion does not unite after its fibres are divided, we should have a fact of great importance. Division of this root would probably be a less serious operation than the removal of the entire ganglion, and might have the same effect in the relief of pain, but the surgical difficulties might be insurmountable. Experiments on animals to determine whether or not the sensory root of the Gasserian ganglion unites after section of its fibres might result in a lessening of the great mortality now existing in operations on the ganglion." Dr. C. H. Frazier has shown that the division of the sensory root may be performed in man, and probably with less danger than the removal of the Gasserian ganglion, as hemorrhage is not so likely to be severe. I should like to lay particular emphasis on the fact that in proposing this operation I did so with much caution. I believe that Horsley is the only one who before Dr. Frazier has divided the roots of the trigeminal nerve without removing the ganglion. Horsley avulsed them at their attachment to the pons, and his patient died seven hours after the operation.[1]

Frazier has cut the sensory root of the trigeminal nerve in a large number of dogs. Seven of these lived sufficiently long for a study of the nervous system by the method of Marchi. The results of my microscopical examination of the nervous systems from these seven dogs are as follows:

Dog No. 4.—Distinct degeneration by the Marchi method is found in the sensory root at its entrance into the pons, and this degeneration is much more intense in the external portion of the root than in the medial portion, although distinct degeneration is also detected in the latter. The motor root in its intracerebral portion shows slight degeneration. A few black dots are present in the mesencephalic root of the trigeminal nerve. In sections from the medulla oblongata the degeneration is especially intense in the dorsal portion of the spinal root, while comparatively few black masses are found in the ventral portion (see Fig. 1). The Gasserian ganglion and the nerve fibres at each end of this ganglion seem to be normal.

Dog No. 5.—The degeneration of the trigeminal nerve is similar to that in dog 4, only it is more intense in dog 5 (see Fig. 2). Both anterior pyramids show slight degeneration. Much degeneration is found in some of the fibres at one end of the Gasserian ganglion, while those at the other end of the ganglion are normal.

Dog No. 6.—The degeneration of the sensory root of the trigeminal nerve in this case is distinct, but is not very intense.

Dog No. 10.—The degeneration of the intracerebral portion of the sensory root of the trigeminal nerve in this case is very indistinct. The nerve fibres at the central end of the Gasserian ganglion are much degenerated, while those at the peripheral end are not degenerated. This degeneration at the central end is probably the result of purulent meningitis.

Dog No. 11.—The degeneration of the sensory root of the trigeminal nerve in this case is present, but unimportant.

Dog No. 12.—The degeneration of the sensory root of the trigeminal nerve in this case is slight. Slight

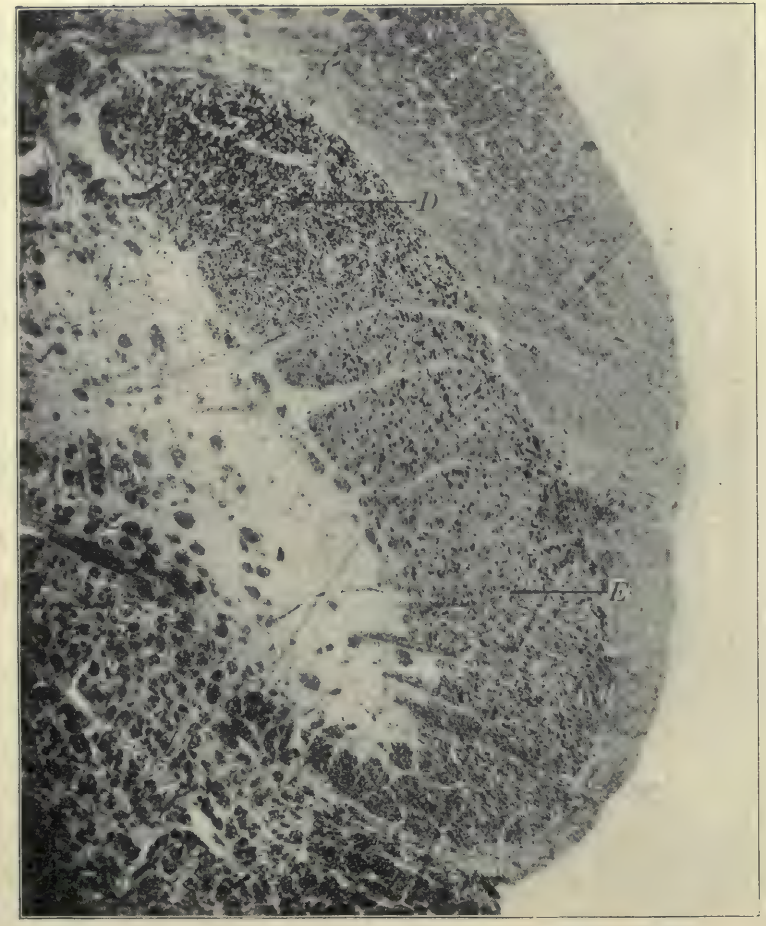

FIGURE 1.—Section of the medulla oblongata from dog 4, showing the descending spinal root. The dorsal portion of this root (D) is much more degenerated than the ventral portion (E), because only the lateral portion of the sensory root was completely divided between the pons and the Gasserian ganglion, as shown in Figure 2. The black dots represent the degenerated fibres.

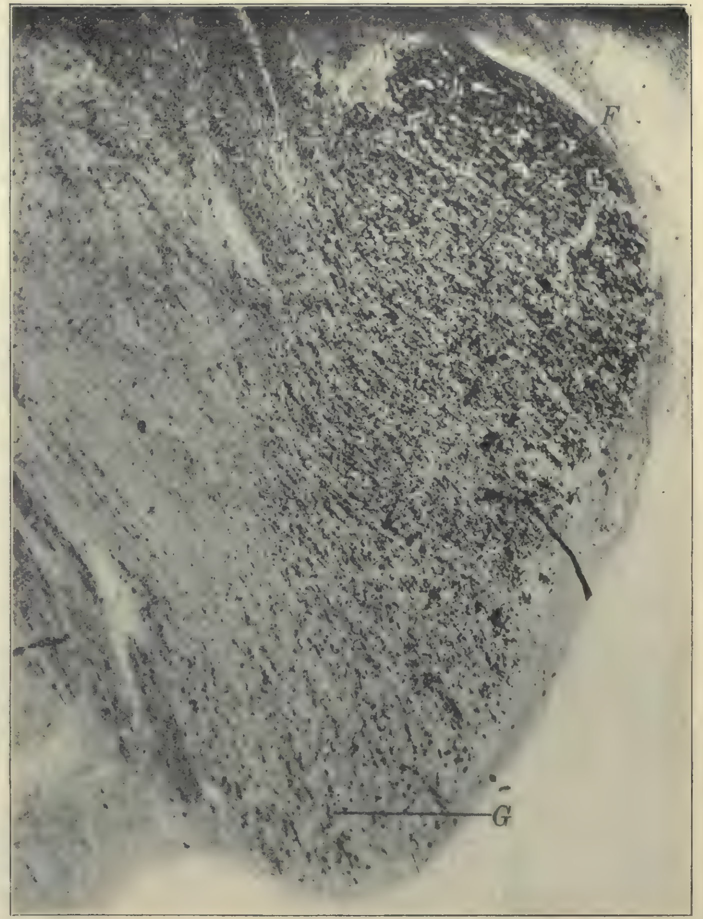

FIGURE 2.—The sensory root at its entrance into the pons, from dog 5. The lateral portion (F) is intensely degenerated, while the medial portion (G) is only slightly degenerated. The degenerated portion indicates the extent of the division of the sensory root. By comparing Figures 4 and 5 it will be seen that the fibres of the lateral portion of the sensory root at its entrance into the pons, in their further course occupy the dorsal part of the descending spinal root.

degeneration is detected in some of the fibres at one end of the Gasserian ganglion.

Dog No. 13.—Degeneration of the sensory root of the trigeminal nerve in this case is not distinct.

Two of these cases, dogs four and five, were especially satisfactory for microscopical study, while the others presented too little degeneration to permit valuable conclusions to be drawn. In dogs four and five it is evident that the lateral portion of the extracerebral sensory root of the trigeminal nerve was cut, while the median portion was only partially injured. In these cases the dorsal portion of the spinal root of the trigeminal nerve was also more degenerated than the ventral. I have not been able in these two cases to detect any attempt at regeneration of the sensory root of the trigeminal nerve, but these cases do not disprove the possibility of such a regeneration. The difficulties of technique in determining by microscopical examination a regeneration of the cut sensory root of the trigeminal nerve are considerable. In removing the brains in dogs four and five the slight connection by means of the motor root between the Gasserian ganglion and the pons was destroyed.

It is important to determine whether regeneration of the central nervous system is possible, and with this object in view an examination of the literature is desirable.

Baer, Dawson and Marshall[2] state that, on the clinical side, so far as they were able to ascertain, no satisfactory cases are reported for man of regeneration and return of function after lesions causing the destruction of any part of the central nervous system. These authors do not discuss the histological evidence of regeneration. They conclude from a few experiments cited from the literature that in the lower vertebrates a certain amount of return of function seems to follow a lesion in the central nervous system, while it is not yet decided certainly whether any such return is possible among higher animals. They experimented on dogs by ligation of the roots of the second cervical nerve between the spinal ganglion and the cord, and from physiological results they conclude that after severance of the fibres of the dorsal root of the spinal nerves between the ganglion and the cord, regeneration of the fibres into the cord will take place under proper conditions, so that normal reflexes through the respiratory, cardiac and vasomotor centres may be obtained. They do not venture to express a positive opinion as to the completeness of the regeneration and the average time necessary for the restoration of function, but their seven experiments showed that great individual differences existed in the rapidity of regeneration. In some cases the return of functional activity in the dorsal root fibres seemed to be nearly complete at the end of ninety days, while in one case the return was far from complete after an interval of 151 days. They conclude that if the posterior root fibres can thus be regenerated in the posterior columns of the cord, there seems reason to hope that the fibres in other tracts may possess the same property, and that therefore it is not impossible that with the proper technique a severed spinal cord might be made to regenerate its broken tracts, both the ascending and the descending. It is much to be regretted that the histological evidence of regeneration of the central nervous system obtained by these investigations of Baer, Dawson and Marshall has not been published.

I hesitate to criticise these carefully performed experiments, but it should be remembered that they do not afford satisfactory evidence that restoration of function after destruction of a part of the central nervous system in man will be complete.

It is presumable that if such restoration occurs in the dog it occurs also in man under similar conditions, but it is only presumable. In these experiments posterior roots were ligated; it would have been better if they had been resected. The divided ends would then have retracted from one another, and the bridge of degenerated tissue caused by ligation of the roots would not have existed. It is possible that such a bridge of tissue may guide the young nerve fibres to the spinal cord.

We know that where only a few sensory fibres exist these may be sufficient to convey impulses coming from the periphery of the body to the central nervous system. Fickler[3] states that in a case of his own, sensation was at one period fully lost but returned after a time to such a degree that almost all qualities became normal, only that warmth and cold sensations were somewhat impaired, and yet very few nerve fibres were found in the posterior and antero-lateral columns of the spinal cord at one level. These few fibres must have been sufficient for the restoration of sensation. The motor tracts of the cord in this case contained more nerve fibres than the sensory tracts, but very little return of motion had occurred. It appears that more normal fibres are requisite for motor function than for sensory.

Fickler also states that Schiefferdecker, Kahler, Stroebe and others have not found any regeneration of nerve fibres worthy of the name after division of the spinal cord in vertebrates. He concludes that the nerve fibres he found within the pia of the spinal cord were regenerated fibres. This conclusion is hardly warranted. Dr. Dercum and I[4] have shown that such fibres may be present in the spinal pia when there is no reason for believing that they are regenerated fibres, and Bielschowsky[5] later has demonstrated the same fact. Bielschowsky also makes the statement that experiments have shown that the spinal cord is not capable of regeneration after it has been divided.

Stroebe's[6] article on regeneration of the spinal cord is especially praiseworthy. After a careful review of the literature on this subject he shows that the opinions of the investigators differ concerning the possibility of regeneration of the cord. Stroebe found from his experiments on rabbits that the nerve fibres of posterior roots that were injured at the level of the lesion in the cord, grow out again from the spinal ganglion toward the spinal cord, and push in a certain distance between the tissue of the scar formation. It was therefore evident that an attempt was made by the posterior roots to penetrate the scar tissue of the cord, but the attempt was not very successful.

The evidence of restoration of the spinal cord being so doubtful, it has seemed to me equally uncertain whether the normal relation of posterior roots to the spinal cord is re-established after these roots have been cut in man. The posterior columns of the spinal cord are largely composed of nerve fibres from the posterior roots, and if these fibres within the cord are not restored after they are divided, it seems probable that the portion outside of the cord, *i. e.*, within the posterior roots, is not restored after these roots are divided. The chief difference between the structure of the intramedullary and extramedullary portions of these fibres, that I am aware of, is that sheaths of Schwann exist on the latter and not on the former, and yet this may possibly be an important difference.

The recent investigations of Bethe[7] may cause us to modify greatly our views regarding the regeneration of nerve fibres. Some investigators in the past have held that the nuclei of the sheath of Schwann have an important rôle in regeneration, but most authorities have taught that regeneration occurs by the outgrowth of axones from the old axones of the central stump of the divided nerve. Bethe has resected the sciatic nerve of the dog, and sewed the peripheral stump within a muscle to prevent union of the two ends. The peripheral end of the nerve degenerated below the point of division of the nerve, but later full regeneration of this peripheral portion occurred from the nuclei of the sheaths of Schwann. The nerve terminated at its proximal end blindly. Irritation of the newly formed nerve caused contraction of the muscles supplied by it, and the regenerated nerve differed in no way from a normal one, and yet it was not in continuity with nerve cell-bodies. If this regenerated nerve were cut, its peripheral portion below the line of division degenerated, but the more central portion persisted even though it were not in connection with nerve cell-bodies. These investigations of Bethe may possibly show that the presence of a sheath of Schwann is necessary for regeneration of a nerve fibre, and may compel us to accept the possibility of regeneration of posterior roots which are provided with sheaths of Schwann, and to deny the existence of regeneration of nerve fibres within the cord which have no sheaths of Schwann, even though they may be the continuation of posterior root fibres. These very experiments make it doubtful, however, whether the posterior roots would be restored beyond the point where the sheath of Schwann ceases, that is, at the entrance of the root into the spinal cord; they may possibly explain why peripheral nerves regenerate so readily while the spinal cord does not.

The nerve fibre of the posterior spinal root has apparently the same structure as the sensory fibre of the peripheral nerve, and yet the reaction of the cell-body in the spinal ganglion is very different according as its central or peripheral process is divided. Investigators (Lugaro, Mering, Fleming, van Gehuchten, Cassirer) have shown that division of the peripheral process of a spinal ganglion cell-body causes very distinct degeneration of this cell-body, or even complete destruction of the cell-body, while Lugaro[8] has demonstrated that the cell-bodies of the spinal ganglia belonging to the sciatic nerve undergo no distinct change when the posterior columns of the cord or the posterior roots belonging to these ganglia are divided. In advanced tabes dorsalis the posterior roots are intensely degenerated even close up to the spinal ganglia, and yet Schaffer, a very careful investigator, has found the cell-bodies of the spinal ganglia normal in tabes by the Nissl method, and I have confirmed his observations. These findings seem to show that the peripheral process of the cell-body of the spinal ganglion has a different importance from that of the central process, and that although a peripheral nerve may be restored after it has been divided, it does not necessarily follow that the nerve fibres of the posterior root will also be restored after they have been divided. What is true of the spinal ganglion cell-body and its processes is probably true of the Gasserian ganglion cell-body and its processes.

We must, therefore, conclude that further study is necessary before we can be convinced that regeneration of sensory nerve roots in man occurs, and that full restoration of function is possible after division of sensory nerve roots. Even if a partial regeneration of these roots were possible, it does not follow that pain would return after division of the sensory root of the trigeminal nerve. There might be a partial return of sensation without pain. We must acknowledge that some evidence of partial return of function in injured posterior roots in animals exists, but no evidence of return of function in the trigeminus after the division of its sensory root is to be found in literature. It is a question whether the fibres of this root could penetrate through the thick bands of the middle cerebellar peduncle and pyramidal tract to the sensory terminal nucelus of the nerve within the pons.

In view of the uncertainty of regeneration of the sensory root of the trigeminal nerve, and of the great mortality in removal of the Gasserian ganglion, the division of the sensory root for the relief of tic douloureux is a justifiable procedure, and I trust we may be able to keep under observation for at least two or three years the patient on whom Dr. Frazier has performed this operation. We are not urging that division of the sensory root should at once replace removal of the Gasserian ganglion, and distinctly recognize that the former operation is on trial.

Frazier has shown by experimentation that the motor root of the trigeminus in the dog may be spared. The possibility of saving this root was present in my mind when I urged that this operation should be tried. The motor root has never been left intact when the Gasserian ganglion has been entirely removed, and it probably never can be. It seems to me a fortunate occurrence that in this first successful operation on the sensory root of the trigeminus Frazier divided the motor root as well as the sensory. All communication between the Gasserian ganglion and the pons was in this way fully destroyed and the best possible conditions were obtained for testing the possibility of regeneration of the sensory root. If this case should be as successful clinically as it has been surgically, we may be able hereafter to relieve the pain of tic douloureux without paralyzing the muscles of mastication,* for Dr. Frazier's operation seems to indicate that he is able to save the motor root; and we may also be able to lessen the danger of loss of vision, inasmuch as by division of the sensory root the nerve cell-bodies of the Gasserian ganglion are left in normal relation with the peripheral distribution of the trigeminus, and changes in the cornea may be less likely to occur. It is not improbable that these cell-bodies exert a trophic influence on the peripheral branches of this nerve. If this operation should be done again it would be well to resect the sensory and motor roots instead of merely dividing them. If it shall be fully established that the sensory root will not regenerate after it is cut, the motor root should be spared.

There are some other conclusions to be drawn from the microscopical study of the nervous system of the dogs operated on by Frazier.

Bregman[9] has obtained results from experiments on the rabbit very similar to my results obtained from the dog. In his cases, where the descending spinal root of the fifth nerve was fully degenerated, the sensory root at its entrance into the pons was also completely degenerated; but where only the ventral portion of the spinal root was degenerated, only the medial portion of the sensory root at its entrance into the pons was degenerated; and where only the dorsal portion of the spinal root was degenerated, only the lateral portion of the sensory root at its entrance into the pons was degenerated. Bregman also found degeneration in the intracerebral portion of the motor root of the fifth nerve after this root was divided, and this was an ascending degeneration in motor fibres. He found also the mesencephalic root of the fifth nerve degenerated.

From the results obtained by Bregman and from mine, we may conclude that the nerve fibres of the sensory root of the fifth nerve, in both its intracerebral and extracerebral portions, maintain the same relative positions throughout the course of this root. This is an important fact, because we may conclude that if the nerve fibres of the sensory root do not mingle freely without regard to order, the nerve fibres of the Gasserian ganglion also probably preserve a definite order of arrangement. The nerve fibres passing distally from the ganglion divide into three distinct divisions at the peripheral end of the ganglion. We can hardly suppose that the nerve fibres within the ganglion are arranged without definite order if in both the sensory root and the

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*** Sufficient time to determine this has not yet elapsed; so far the case has been very successful clinically.**

peripheral divisions a very definite arrangement exists. Tiffany's suggestion to spare the inner third of the ganglion in order to preserve vision seems, therefore, to have an anatomical basis, although it is not improbable that if this inner third of the ganglion were preserved when the other two-thirds of the ganglion were removed, the relief of pain would not be permanent.

PART II.

BY CHARLES H. FRAZIER, M. D.

INTRODUCTION.

The surgery of the Gasserian ganglion has received a great impetus during the past few years, largely through the efforts of those who by the most careful study of the anatomical relationships of the structures in and about the field of operation have been successful in surmounting many of the operative difficulties. All the improvements in technique, for a practical consideration of the subject, may be grouped under two headings: (1) those which render the ganglion easier of approach, and (2) those which suggest means, not of controlling, but of preventing hemorrhage. The pterygoid route of Rose and the temporosphenoidal route of Doyen have practically been abandoned in favor of the temporal route first advocated independently by Hartley and Krause. In order to lessen the risk of injuring the middle meningeal vessel and to facilitate the exposure of the ganglion Cushing suggested a modification of the Hartley-Krause operation, which he has called the infraarterial route. The base of the flap corresponds to the level of the zygoma and the trephining opening is sufficiently low to escape the sulcus arteriosus in the anterior inferior angle of the parietal bone, which lodges the middle meningeal vessel, and to give the maximum exposure with the minimum of cerebral compression. Sapejko (*Revue de Chirurgie*, September, 1901) goes so far as to recommend the removal of the great wing of the sphenoid up to and including the foramina rotundum and ovale.

No matter what the method of approach, each of these operations has for its object the removal or avulsion of the Gasserian ganglion and the adjacent portions of its first, second and third divisions. I am about to describe an operation for the relief of tic douloureux which depends for its success not upon the removal of all or part of the ganglion, but solely upon the division of its sensory root. This plan of operation, so radically different, was suggested to me by Dr. William G. Spiller almost three years ago. Granting for the time that from the operator's standpoint this measure could claim many points of advantage over those procedures which entail the removal of the ganglion itself, I withheld my endorsement until I was convinced that regeneration of the nerve fibres at the point of division was doubtful, and, that, in view of this uncertainty, therefore, this operation might be justified. In order to demonstrate experimentally that regeneration would not take place, I conducted, in connection with my colleague, Dr. Spiller, a series of experiments in which the proposed operation was practised upon dogs. The interpretation of the results of these experiments and their significance from the standpoint of the neuropathologist is carefully considered in Dr. Spiller's contribution in this paper. Suffice it to say here that Dr. Spiller is of the opinion that the burden of evidence is still with those who would prove that regeneration of fibres with restoration of function does follow division of these sensory roots.

OPERATION.

The following are the steps of the operation:

1. Reflection of a horseshoe-shaped flap of skin and subcutaneous tissue. The flap corresponds in width to the length of the zygoma; its base is on a level with the lower border of the zygoma, its convexity reaching a point 6 cm. above.

2. Division of the zygomatic processes of the malar and temporal bones. After reflection of the superficial flap of skin and subcutaneous tissue an incision is made in the periosteum over the middle of zygoma throughout its length and the periosteum elevated sufficiently to allow of the introduction of the bone-cutting forceps and the division of the zygomatic processes of the malar and temporal bone.

In my operations upon dogs, where the field of operation was so much smaller than that of the human subject, and where the bellies of the temporal and masseter muscles were proportionally so much larger, I found it absolutely necessary to resect the zygoma in order to be able to retract the temporal muscle sufficiently to allow of a proper exposure of the field of operation and I determined to introduce this step into the technique of my next operation upon the human subject. It is better to practise a temporary rather than a permanent resection of the zygoma. At first thought one might think it inadvisable to replace the segment on the grounds that the bone might not become united owing to the difficulty of keeping it at rest. One would realize how unlikely it is that this will occur if one takes into consideration that the most likely cause of displacement, muscular action, is not operative because the muscles attached to the fragment of bone and concerned in the act of mastication will have been deprived of their motor nervous supply, which is derived from the inframaxillary branch of the trigeminus, before the operation has been completed. (This assertion is based upon the assumption that the integrity of the motor root of the ganglion has in but very few instances been preserved.) One or two sutures introduced at either end of the fragment through the periosteum will suffice to insure fixation until union occurs. Necrosis of this fragment has been recorded as a possible unfavorable complication of temporary resection, but this can be avoided if one bears in mind that the bone receives a liberal blood supply through the periosteum and avoids stripping this structure from the bone except at the points where the bone-cutting forceps have to be applied.

3. Reflection of a horse shoe-shaped flap, composed of temporal fascia, muscle, zygoma and pericranium, corresponding in shape to the superficial one but of somewhat smaller dimensions. This flap is reflected sufficiently to expose to view the temporal fossa; during the operation it will be subjected to considerable traumatism consequent to the constant traction and pressure and will be swollen and tender for a short time. Owing to the contractile character of the tissue of which it is composed the flap will shrink at least one-third before the operation is completed so that some little traction will have to be made in order to approximate the edges upon closure of the wound.

4. Removal with the trephine of a button of bone at a point corresponding to the middle of area exposed and enlargement of the opening with the rongeur forceps until its diameter measures three to four centimetres. The usual precaution must be taken in trephining here as in any portion of the calvarium where the bone is of such variable thickness, in order to avoid injuring the dura; and additional precautions are necessary in this region owing to the fact that the middle meningeal artery lies immediately beneath the button of bone to be removed. With the rongeur forceps the trephine opening is enlarged about equally in all directions and should extend downwards to the level of the crista infratemporalis.

5. Separation of the dura and exposure of the ganglion and its sensory root. The adherent dura is separated by blunt dissection (the handle of a scapel enveloped in a single layer of gauze will meet all indications) inwards and forwards until the foramen ovale or rotundum comes into view, either of which serve as a guide to the site of the ganglion. This is the most tedious stage of the operation and one which taxes the patience of the operator to the utmost. Hemorrhage now constitutes the great bugbear. Protracted and persistent oozing follows the separation of the dura from every point at which it is adherent to the skull; the older the patient the firmer the adhesion and the freer the hemorrhage. Hemostasis can be effected only by pressure and heat; small pledgets of gauze saturated with a hot saline solution are cautiously applied to the bleeding point and allowed to remain for periods of two to five minutes. In my series of operations upon dogs I tested the efficiency of gelatin in 5 per cent solution as a hemostat in intracranial operations with practically negative results. The solution had no apparent effect. The dura is most adherent to the skull at the margins of the foramina so that the most troublesome bleeding is not experienced until one has arrived almost at the site of the ganglion. Second only to hemorrhage as a troublesome feature of this stage of the operation is the presence of large bony eminences on the floor of the middle fossa. As pointed out by Amyx these eminences are more commonly met with in heads not having a great transverse diameter between the ears, but whose external bony prominences are well marked rather than in those skulls with a large transverse width; these prominences are situated usually external to the foramina ovale and rotundum and if very large will have to be chiselled off in order to expose the foramina to view and remove the ganglion In some cases the ganglion itself lies beneath a bony roof as though it were a continuation of the petrous portion of the temporal bone. While this is an anomaly in men it is not so in the dog. Almost without exception in the series of dog's skulls which I had an opportunity to examine while carrying on the experimental work, the ganglion was covered by a thin shell of bone which had to be removed in order to bring to view the ganglion and its sensory root.

With hemorrhage well enough under control to enable one to recognize the anatomical landmarks, the operator makes an incision into the dura and dura propria between the foramen ovale and spinosum and with a blunt dissector separates the dural envelope from the upper surface of the ganglion as far back as may be necessary to expose to view the sensory root.

6. Up to this point the method of procedure has not differed essentially from those operations which have in view the extirpation of the ganglion. From now on the courses diverge: in the one the operator proceeds to liberate and extract the ganglion and its branches, in the other to liberate and divide the sensory root. The division of the root is not a difficult performance. When fully exposed it is picked up on a blunt hook (see Fig. 1), which is passed around the nerve from without inwards. The nerve is divided either by making traction with the hook or cutting directly upon the hook with knife or scissors. It would be a better plan, however, and I will carry it out in future cases, after elevation of the nerve upon the hook to grasp it with a pair of forceps, hemostatic or dissecting, and remove a small section with knife or scissors. This slight modification will add nothing to the dangers and little to the difficulties of the operation and will serve a two-fold purpose, on the one hand furnishing a specimen for a pathologic examination and on the other leaving a defect in the continuity of the nerve which would render regeneration a possibility still more remote.

In connection with this step of the operation, there is one point which will naturally come up for discussion. Can the sensory root be isolated from the motor root so that the integrity of the latter may be preserved? This question may be answered in the affirmative if certain reservations be made. That it is possible upon the living subject to separate the motor from the sensory root was proven by my own case. I had practically concluded the operation and was about to close the wound; in order to assure myself that none of the fibres of the sensory root had been left undivided, I repeated the last step of the operation and in so doing I picked up the motor root which up to this time had remained intact, and unintentionally divided it. It is *possible*, therefore, to divide the sensory without the motor root; whether we can attain sufficient dexterity to avoid the accident which happened in my case is a matter to be settled by future repeated observations.

7. Closure of the wound.—The section of zygoma is returned to its normal situation and secured in place by one periosteal suture at either end. While there is no danger of displacement as a result of muscular action, the fragment may be dislodged during the application, or the changing, or the pressure of the dressing and for this reason the introduction of a suture at either end is recommended. A narrow strip of gauze enveloped as it passes by the scalp in a cuff of rubber tissue is introduced for drainage. If the bleeding is free at the conclusion of the operation it must be controlled by pressure with strips of gauze. The rubber tissue, by preventing the edges of the scalp wound adhering one to the other, will insure perfect drainage. The wound in the temporal muscle and fascia is closed with buried interrupted catgut sutures, and the superficial wound with interrupted silk-worm gut sutures.

A special protective dressing is applied to the eye in order to prevent corneal ulceration.

Remarks.

Whether this operation for the relief of tic douloureux will receive the endorsement of the surgical profession and take the place of the operation now in vogue, will depend altogether upon the acceptance without reservation of the facts embodied in the following two assertions: (1) Regeneration of the sensory root will not take place after its division; and (2) (*a*) Liberation and division of the sensory root, obviating many of the operative difficulties associated with the liberation and extraction of the ganglia, is easier of execution; (*b*) the integrity of the structures of the cavernous *sinus* is not endangered; (*c*) the operation should be attended with a lower mortality.

I will not enter into the discussion of the subject of the regeneration of the sensory roots of the cranial ganglion as this is a problem which should be left to the neuropathologist for solution and in this paper has been very carefully and exhaustively treated by Spiller. It remains for me to substantiate the claims which have been advanced from the surgical aspect.

Every surgeon will frankly admit that hemorrhage is the greatest bugbear in operations upon the Gasserian ganglion and holds it accountable for many failures and many fatal issues. The bleeding that takes place during the operations in this field might be said to be either troublesome or alarming: troublesome when it follows division of the middle meningeal artery, the emissary veins; alarming when due to laceration of the cavernous sinus. Let us consider the various sources of hemorrhage separately. Hemorrhage from the middle meningeal artery, since the adoption of the infraarterial route, will occur infrequently and when it does, may be controlled by plugging the foramen spinosum with gauze or, as Krause has suggested, with

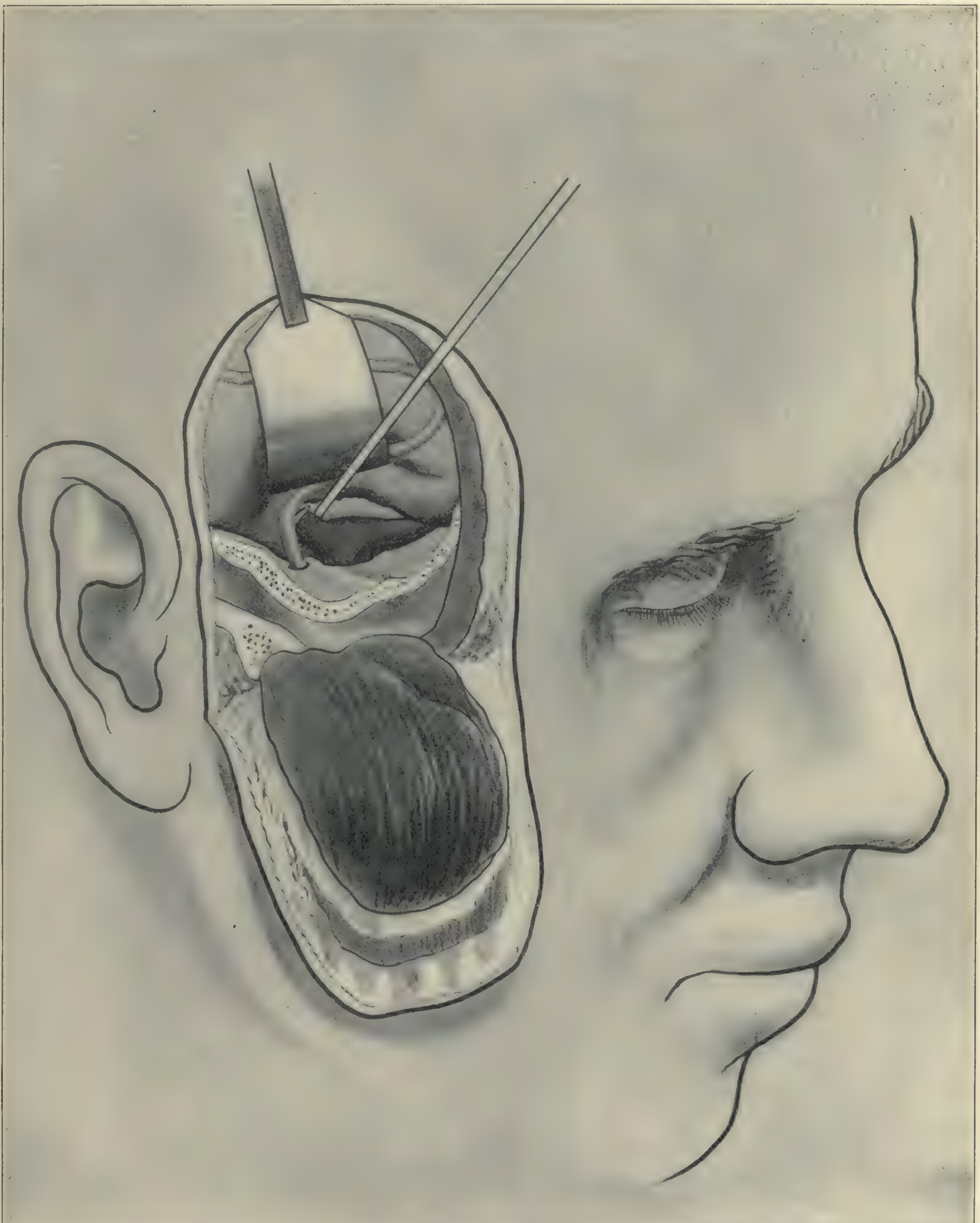

FIG. 1.—Illustrating the final step of the operation. The sensory root is picked up with a blunt hook preparatory to its division. The drawing, made directly from a dissection upon the cadaver, shows the reflected dura propria and the relation of the foramina rotundum, ovale and spinosum, and the middle meningeal artery to the ganglion and its sensory root

the end of a blunt hook (Krause has had constructed a series of hooks of various sizes which he keeps on hand to meet this emergency). If, in enlarging the opening in the skull, the operator should resect that portion of the skull containing the sulcus arteriosus, he runs the risk in the removal of that segment of bone of wounding the vessel. As it is not necessary, in order to expose the ganglion, to carry the resection so high, injury to the vessel at this stage of the operation should be regarded as a blunder. The vessel will most likely be injured at its other fixed point, namely the foramen spinosum. If too great traction be made upon the vessel at this point in elevating the brain, or if too great force be applied in separating the dura in the neighborhood of the foramina where the attachments are firmest, the vessel is in imminent danger of being lacerated. Experience alone teaches one how much force can be applied to these structures without endangering their integrity. In so far as the middle meningeal artery is concerned, neither of the two operations under discussion can claim an advantage over the other. Hemorrhage will follow the separation of the dura from the various places at which it is attached to the skull; it is very variable in quantity, the degree of hemorrhage seeming to be in proportion to the number and firmness of the dural attachments. From this source bleeding is, to say the least, annoying but can always be controlled by pressure. The nearer one approaches the ganglion the firmer the adherence of the dura, the correspondingly freer the bleeding. In as much as the ganglion receives its largest blood supply from below, surgeons are advised in performing those operations which are designed to remove the ganglion, to put off the elevation of the ganglion till the latest moment in order, as Cushing says, to postpone what degree of hemorrhage is unavoidable as long as possible. In this particular, therefore, one can justly claim for the operation which leaves undisturbed the attachments of the ganglion to its unyielding base, an advantage over one the execution of which invades this source of free and troublesome hemorrhage. The time required to separate the ganglion from its base and the additional time required to control or check the flow of blood before the operation can be proceeded with, must be taken into consideration and given due weight in the estimation of the relative merits of the operations under discussion.

The third source of hemorrhage is the cavernous sinus, and, as has been already said, should any injury happen to this sinus bleeding may be so profuse as to give cause for alarm. The sinus is exposed to danger once the operator begins to free the internal aspect of the ganglion, and in this connection Cushing says "that it is well to conduct these manipulations *as near as possible to the sensory root, since that is the safest point*, and one at which there is less likelihood of injuring the cavernous sinus and sixth nerve." Therefore, in limiting our field of operation to the posterior aspect of the ganglion and its sensory root, we confine our manipulations to the point of greatest safety. So much stress would not be laid upon the superiority of one operation which is associated with less bleeding than another, because the amount of blood lost in either is not a menace to life and will not very materially affect the ultimate results, but because the control of hemorrhage necessary to the continuance of the operative maneuvers is only effected after repeated application of pressure for various periods of time, which in the aggregate may rightly be considered as a factor unfavorably influencing the results. Patients of advanced years, and most of the sufferers of trifacial neuralgia that come to us for operation have reached that period of life, are not good subjects for prolonged general anesthesia, therefore any measure which will economize time should, other things being equal, carry some weight with it. Thus far I have aimed in drawing a comparison to throw the balance in favor of the operation requiring less time for its completion and attended with less hemorrhage. I now call your attention to the operative difficulties and dangers that are avoided by stopping short of the extraction of the ganglion. It goes without saying that the exposure of the ganglion is by far less difficult than its extraction. The ganglion and its three divisions are so firmly bound down to the base of the skull that the liberation of the structures is the step of the operation which, above all others, tests the skill, dexterity and patience of the operator. For the completion of this step of the operation one begins by exposing the superior surface (to quote Cushing again) "of the stellate structures well back onto the sensory root." Without going a step further, without exciting one whit more hemorrhage, without running any further risk of injuring adjacent structures, we have made all the preparation necessary for division of the sensory root. Thus one operation is practically complete before those difficulties, both serious and troublesome, common to the other operations have been encountered. Not only, then, do we obviate certain operative difficulties, but we are able as well to eliminate certain dangers to adjacent structures. In practically every operation in which the ganglion has been removed the motor root has been destroyed, but from what has already been said in discussing the last steps of the operation we not only believe it possible to divide the sensory without the motor root, but were able to demonstrate this on the living subject. Too much importance, it seems, has been attached to the question of the preservation of the motor root, since its division causes only the little annoyance to the patient that follows paralysis of the muscles of mastication on one side. The patient can chew his food only on the unaffected side. However, if it is possible to save the nerve, we are not justified in deliberately sacrificing it, and if the neuralgia involve both the right and left trigeminus, what is only an annoyance in a unilateral case becomes in the bilateral a serious complication.

As the motor root, so the sixth nerve is almost always injured during the extraction of the ganglion; its proximity to the ophthalmic division is such that division of one without the other is practically impossible.

Although a positive assertion cannot be made, there are some grounds for believing that trophic disturbances in the cornea secondary to division of the first root or the ganglion itself may not follow the division of sensory root because of the probable presence in the ganglion of trophic centres presiding over the peripheral nerve. In the case which is reported in this paper, there was not a suspicion of a keratitis, although a very simple dressing, consisting of a compress saturated with boracic acid, was applied to the eye, and this for only one week following the operation.

On the assumption that we are recommending an operative procedure which obviates many difficulties and some dangers, which is easier of execution, comparatively speaking, and economical as to time, it is reasonable, at least, to prophesy a greater reduction in the mortality than that which has resulted from the improvements in technique which have within the past two years been suggested.

CONCLUSIONS.

As a substitute for all operations which depend for their success upon removal of all or a part of the ganglia, I recommend an operation which depends for its success solely upon the division of the sensory root of the ganglion. Granting it will effect a radical and permanent cure, the advantages of this operation are the following:

1. It should be attended with a lower mortality.
2. It obviates a number of difficulties.
3. Its execution is, comparatively speaking, simple.
4. It is practically complete when the posterior aspect of the ganglion and its sensory root have been exposed; that is, it is practically complete before the difficulties most serious and troublesome common to other operations have even been encountered.
5. The integrity of the cavernous sinus is never in danger.
6. The risk of injuring the sixth nerve is avoided.

CLINICAL REPORT.

The following is a brief history of the case upon which I performed this operation:

J. L., aged sixty-eight, was referred to my service in the University Hospital by Dr. D. J. McCarthy.

Family History.—Father and mother died from typhoid fever, one brother and sister living and well, two brothers died from unknown causes. His wife, four sons and one daughter are living. One son and one daughter are subject to attacks of supraorbital neuralgia; one son died from phthisis.

Previous History.—Had the usual diseases of childhood. About ten years ago had an attack of sciatica which lasted for some seven months, but did not confine him to bed.

Social History.—The patient was born in Ireland and came to the United States thirty-four years ago. Has been a hard worker ever since ten years of age. His occupation formerly was that of fireman; at present he is a watchman. Has never used alcohol excessively, occasionally taking a glass of liquor, which he found increased his neuralgic pains. No venereal history.

History of Present Illness.—About five years ago he first began to have sharp shooting pains referred to the course and distribution of the right supraorbital nerve, beginning at the supraorbital notch and extending up over the forehead as far back as the anterior edge of the parietal bone. These attacks were provoked by exposure to cold, dampness or wind. Four years ago a neurectomy of the supraorbital nerve was performed, after which he enjoyed a period of relief. Within a year of this operation the pains recurred with their former severity, when the second peripheral operation was performed. The latter afforded him relief for about six months; and since that time a third and fourth operation have been performed. Each succeeding operation seemed to afford him relief for a shorter period of time. The administration of large doses of salicylates had beneficial results for a while.

Condition on Admission.—Examination of the thoracic and abdominal organs negative.

Examination of the Head.—The area of tenderness extends on the right side of the head backward from the supraorbital margin a distance of 13 cm., and from the median line a distance of 8 cm. The area of anesthesia is 2 cm. wide anteriorly and 5 cm. wide posteriorly, and its inner margin is 1.5 cm. to the right of the median line.

Examination of the Eye.—Hypermetropia and astigmatism; no coarse changes.

Urine Analysis.—Clear, amber, acid, light flocculent precipitate, specific gravity 1019, urates and mucus, no albumin or sugar.

October 12, 1901. Operation. Division of sensory root of Gasserian ganglion.

October 17, 1901. Examination of patient under this date reveals complete anesthesia over the area corresponding to the distribution of the trifacial nerve (see Fig. 2).

November 2, 1901. Patient was discharged from the Hospital to-day. During the post-operative period nothing occurred worthy of note.

Examination under present date reveals absence of the supraorbital reflex on the affected side. The area of anesthesia extends back from the supraorbital margin 18.5 cm. and 3.5 cm. to the right of the median line at this level. The zygoma has become firmly united. There are no corneal ulcers of the eye of the affected side.

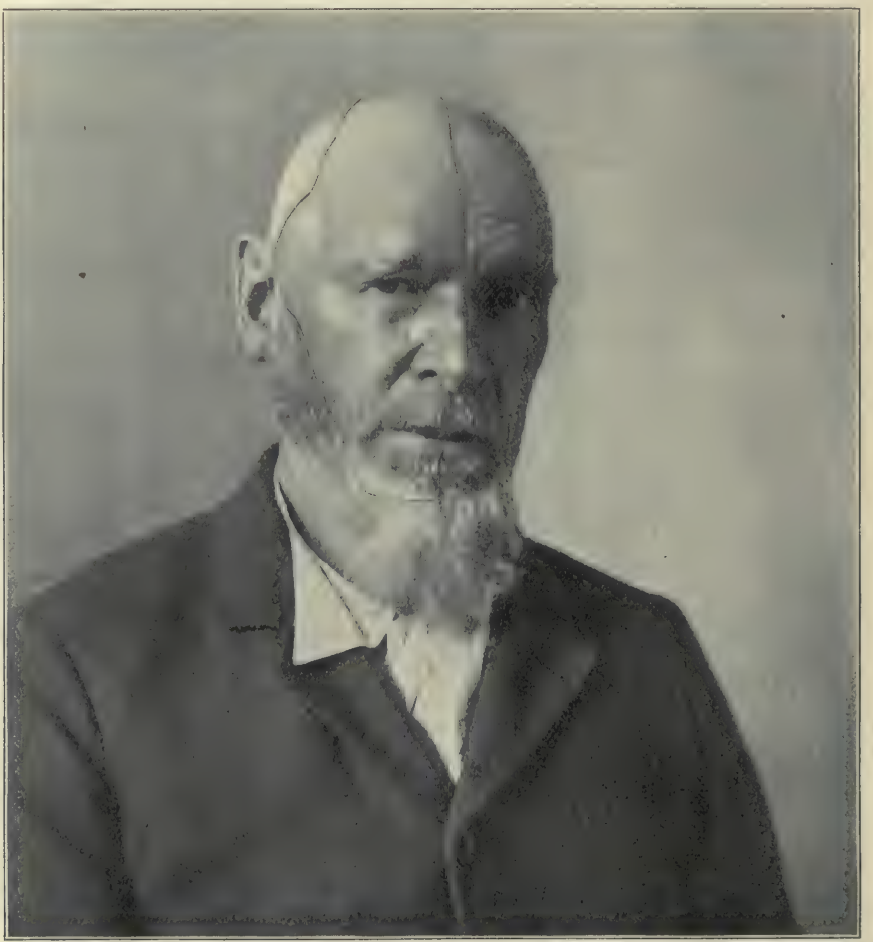

FIG. 2.—Showing area of anesthesia one week after division of the sensory root of the trigeminus.

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A FURTHER REPORT UPON THE TREATMENT OF TIC DOULOUREUX BY DIVISION OF THE SENSORY ROOT OF THE GASSERIAN GANGLION.*

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and

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REMARKS BY DR. FRAZIER.

In June, 1901, I reported to the Surgical Section of the American Medical Association, then in session at St. Paul, the results of a series of experiments upon dogs conducted by Dr. Spiller and myself with a view toward determining the feasibility of dividing the sensory root of the Gasserian ganglion for the relief of tic douloureux or trifacial neuralgia. In December of the same year I reported to the Academy of Surgery of Philadelphia my experience in the performance of the operation upon the human subject. But two months had elapsed between the time of operation and the announcement of the results, and while at that time there was absolutely no recurrence, I did not feel as though sufficient time had elapsed to warrant my considering the relief as permanent. As this operation had been performed but once upon the human subject, and as it overcomes many of the difficulties besetting the extirpation of the ganglion, it is only proper that the record of the case should be made public now that after the lapse of a year the time has arrived when we can justifiably regard the recovery as permanent.

The history of the case is briefly as follows:

A male, aged 68 years, had been a sufferer from neuralgia of one or more of the branches of the trifacial for a period of five years, during which time he had undergone 4 peripheral operations. In October, 1901, in the surgical clinic of the University Hospital, I divided the sensory root of the Gasserian ganglion. Convalescence was uninterrupted and on the 2d. of November the patient was discharged from the hospital. At this time there was complete anesthesia over the area corresponding to the distribution of the trifacial nerve, there had been no recurrence of the neuralgic attacks, there were no corneal ulcers on the eye of the affected side. In other words, the immediate operative results were perfect. Recently, Dr. D. J. McCarthy, who had referred the case to me, made, at my request, a thorough examination of the patient, the pith of which I take pleasure in presenting to you. The area of anesthesia corresponds in extent to that recorded upon his discharge from the hospital; the cornea and conjunctiva on the affected side are completely anesthetic; there has been no recurrence of pain and the patient's mental state reveals marked improvement since the operation.

This, briefly, is the clinical record of the case to the consideration of which I invite your attention. Having reviewed the history of the operation and alluded to the history of one successful case, there remains to review the *rationale* of the operation and its claim of superiority over the only other radical treatment, that of complete extirpation of the ganglion. The operation depends for its immediate success upon the complete division of the sensory root of the Gasserian ganglion, and for its permanent success upon what may be called the inability of this root to undergo regeneration. Dr. Spiller made a careful microscopical examination of seven specimens of the Gasserian ganglion and its roots, removed from as many dogs upon whom I had practised division of the sensory root, and although these experiments were not fully as satisfactory as could be desired, as a result of his studies he concluded that "further study is necessary before we can be convinced that regeneration of sensory nerve roots in man occurs, and that full restoration of function is possible after division of sensory nerve roots." Not only is this conclusion warranted by the experimental work above alluded to, but it is a logical deduction of the experiments and investigations of other observers. Granting, then, that from the standpoint of the neuropathologist the *rationale* of this operation is based upon a foundation supported by sound and scientific reasoning, it remains for me to enumerate and demonstrate the advantages claimed for division of the sensory root as against the extirpation of the ganglion.

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*The patient was presented at a meeting of the College of Physicians of Philadelphia, Oct. 1, 1902.

**From the William Pepper Clinical Laboratory, Phoebe A. Hearst Foundation.

1. It obviates a number of difficulties. Every surgeon will frankly admit that hemorrhage is the greatest bugbear in operations upon the Gasserian ganglion and will hold it accountable for many failures and many fatal issues. Hemorrhage occurs, generally speaking, from three sources: (a) From the middle meningeal artery, (b) from the emissary veins, (c) from the cavernous sinus. In the first two instances hemorrhage may be described as only troublesome, but in the last as alarming. In so far as the middle meningeal artery is concerned, neither of the two operations under discussion can claim an advantage over the other.

As to the second source of hemorrhage, this seems to be in proportion to the number and firmness of the dural attachments. The nearer we approach the ganglia, the firmer the adherence, and the correspondingly freer the bleeding. Inasmuch as the ganglion receives its greatest bloodsupply from below, surgeons are advised, in preparing to extirpate the ganglion, to put off elevation of the ganglion till the latest moment in order to postpone what degree of hemorrhage is unavoidable. In this particularly one can justly claim for the operation, which leaves undisturbed the attachments of the ganglion to its unyielding base, an advantage over one, the execution of which invades this source of free and troublesome hemorrhage. Not only is this source of bleeding avoided, but a considerable amount of time is saved which would be required to separate the ganglion from its base and to control the bleeding while this step of the operation is being performed. Hemorrhage of a serious and alarming nature follows injury from the cavernous sinus. This vascular channel, being in intimate relation with the internal aspect of the ganglion, is exposed to danger once the operation begins to free it from the ganglion. Confining, as we do in practising division of the sensory root, our manipulations to the root itself and to the posterior aspect of the ganglion, we work at the point of greatest safety in so far as the cavernous sinus is concerned. Granting that in the operation which has for its aim and object simply division of the sensory root we avoid sources of hemorrhage both troublseome and alarming, necessarily invaded in practising extirpation of the ganglion, we pass on to the consideration of other operative difficulties that give us no concern if we stop short of the extraction of the ganglion.

It goes without saying that the exposure of the ganglion is by far less difficult than its extraction, and that the extraction of the ganglion is the step of the operation which, above all others, tests the skill, the dexterity and the patience of the operator. The ganglion and its three divisions are so firmly bound down to the base of the skull that their liberation is of itself a most perplexing undertaking. Once the ganglion is exposed, we have made all the preparations necessary for the division of the sensory root without going a step further, without exciting one whit more hemorrhage, without running any further risk of injuring adjacent structures. In other words, one operation is practically complete before those difficulties common to the other operation have been approached. So much for the avoidance of difficulties. Secondly, **the avoidance of injury to adjacent structures,** more particularly (a) the motor root of the ganglion, (b) the sixth nerve and (c) the cavernous sinus. As to the latter, allusion has already been made to the manner in which the possibility of injury to this structure is reduced to a minimum by leaving undisturbed the internal aspect of the ganglion. As to the motor root of the ganglion, my experience goes to prove that it is quite possible to divide the sensory root without disturbing the motor root. On the other hand, in practically every operation in which the ganglion has been removed the motor root has been destroyed. Its destruction causes such annoyance to the patient as would follow paralysis of the muscles of mastication on the affected side. Should the neuralgia involve both right and left trigeminus, what is only an annoyance becomes a serious complication. The sixth nerve, or *abducens*, is in such intimate relation with the ophthalmic branch that division of one is almost impossible without division of the other, and inasmuch as in extirpation of the ganglion each peripheral branch must be divided, it is a matter of great difficulty in performing this operation to save this cranial nerve. The third claim for the operation is a **reduction in the rate of mortality.** The operation has not been generally adopted, and there are no statistics at hand upon which to estimate the mortality. But from our knowledge of the conditions that affect the mortality-rate in other operative procedures, it is only reasonable to predict that the operation which is the more economical as to time, which is attended with considerably less hemorrhage, which avoids injury to important structures adjacent to the field of operation, which involves in its performance less tissue traumatism and indirectly eliminates the predisposition to infection, which is, comparatively speaking, easy of execution —I say it is reasonable to predict that this operation will lower the mortality-rate. During the past two or three years such have been the improvements in the technique that the mortality is already materially reduced, so that we need no longer regard operative attacks upon the Gasserian ganglion and its roots as belonging to the desperate "kill or cure" class of surgical measures.

I have already received so many inquiries from surgeons in various parts of the country that I am disposed to believe this modification of the surgical treatment of trifacial neuralgia is now being given a very fair trial and may be eventually adopted. All that has been claimed for the newer operation is based upon substantial evidence. The whole idea from its conception has been developed in a perfectly logical manner: its development has been the result, first, of *a priori* reasoning, then of experimentation upon the lower animals, then upon a painstaking neuropathological study into the question of regeneration of the central nervous system, then upon the elevation of a technique and, finally, upon the performance of the operation upon the human subject, with its successful issue.

REMARKS BY DR. SPILLER.

My observation of a number of operations, the aim of which has been the removal of the Gasserian ganglion, has deeply impressed me with the difficulties of the procedure usually resorted to by the surgeon in his final effort to obtain relief from the sufferings of tic douloureux. The mortality of Gasserian ganglion operations, as given by Tiffany, 22.2 per cent., is so great that the neurologist refers his patient with tic douloureux to the surgeon with hesitation; and yet the pain is so intense that often the patient is willing to take any risk in his endeavor to obtain relief. The temptation to suicide in some cases is very real. It is not unlikely that many unsuccessful or fatal cases are never reported, and that the mortality of the operation is greater than that given by Tiffany.

Having these facts in mind, I suggested in a paper published in collaboration with Dr. W .W. Keen, in 1898, that division of the sensory root of the trifacial nerve[1] would probably give the relief from pain that might be hoped for from the removal of the Gasserian ganglion, and probably would be a less serious operation. I requested Dr. Frazier to employ this method in a case of tic douloureux, and here I take the opportunity to express my satisfaction that the division of the sensory root of the trifacial nerve has been done in this first case by so skilful a surgeon. Had any failure occurred at this time, the operation might have been rejected as impracticable.

Even the division of the sensory root is so formidable an undertaking that one cannot resort to it lightly, and he may justly demand the evidence on which the operation is based. In the paper published in 1901 by Dr. Frazier and myself[2], I endeavored to show that the possibility of regeneration of the sensory root of the trigeminal nerve after division is remote, and it is not necessary to reiterate what was said at that time. I have shown that, while peripheral nerves usually regenerate freely, it does not follow necessarily that the sensory root of the Gasserian ganglion or the sensory root of the spinal ganglion behaves in a like manner. The investigations of Bethe[3] lead us to believe that only those nerve fibers that are supplied with sheaths of Schwann have the possibility of regeneration. Startling as the statements of Bethe are, they have been confirmed by Ballance and Stewart[4], and in these statements we have an explanation why regeneration is common in peripheral nerves and rare, if it occurs at all, in the nerve fibers of the central nervous system, inasmuch as the latter possess no sheaths of Schwann. Ballance and Stewart, after performing a large number of experiments, reject the views on regeneration so widely held, viz., that the new axis cylinders in a regenerating nerve are direct outgrowths of the axis cylinders in the central segment of the divided nerve, and they hold that the new nerve fibers in the distal segment of a divided nerve—axis cylinders, medullary sheaths and neurilemmata—are formed from pre-existing cells in the distal segment itself. In the distal segment of a nonunited nerve, regeneration of axis cylinders and of medullary sheaths takes place, although full maturity of the nerve fibers is not attained unless the distal segment be joined to the proximal, so that their fibers may become functionally continuous. The neurilemma cells take on an active neuroblastic function and give rise to new axis cylinders.

This remarkable confirmation of Bethe's findings causes us to believe that the former teaching concerning regeneration of nerve fibers must have been incorrect, and in the acceptance of an almost abandoned theory, now revived, we probably have the explanation for the durability of the relief from pain in the patient on whom Dr. Frazier has operated.

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[1] Keen and Spiller, American Jour. of the Med. Sciences, Nov. 1898.

[2] Spiller and Frazier, Philadelphia Med. Journal, 1901, No. 2.

[3] Bethe. Abstract in Centralblatt fuer Nervenheilkunde und Psychiatrie, July 1901, p. 440.

[4] Ballance and Stewart, "The Healing of Nerves," Macmillan and Co., 1901.

If nerve fibers have grown out from the nuclei of the sheaths of Schwann of the sensory root of the trifacial nerve in this case—and that is doubtful—they evidently have not been able to extend beyond the portion at which the sheaths of Schwann cease, namely at the entrance of the root into the pons. The motor root in this patient has not been restored any more than the sensory, for there is still paralysis of the muscles of mastication upon the operated side.

It may be urged by some that one year is not sufficient time for a determination of the permanency of the relief in this case, and that, even after one year, return of pain has occurred after peripheral resection of the trifacial nerve. I doubt very much whether pain has first recurred after a year in any case in which the anesthesia in the area of the resected nerve has been complete one year after resection, or the muscles of mastication remained paralyzed so long a time. The course of the nerve is not destroyed by peripheral resection, and the relation of the parts are such that the surrounding tissues afford a means of conduction for the young nerve fibers. This is not the case after division of the sensory root of the trifacial nerve. The peripheral end of the divided root doubtless retracts, and it is not probable that the delicate young nerve fibers—if we grant that they are formed at all—could find their way across the subdural space and penetrate the dense transverse fibers of the middle cerebellar peduncle, and the longitudinal fibers of the pyramidal tract to reach the sensory nucleus of the trigeminus situated deep within the pons, and thereby establish a connection with the brain.

I would urge that in future operations the sensory root should be divided close to the pons, so as to leave no part of the root containing sheaths of Schwann in connection with the pons, and that as much of the root should be resected as can conveniently be cut.

The absence of all corneal changes in the case operated on by Dr. Frazier seems to indicate that the Gasserian ganglion may exert a trophic influence over the peripheral branches of the trigeminus and, if this be true, the leaving of the ganglion *in situ* has another very decided advantage. The hope of avoiding ocular complications was one of my inducements for urging the division of the sensory root.

We may expect some paresthesia, as numbness, to be felt in the face after the operation on the sensory root, just as it occurs after removal of the Gasserian ganglion, but this is not pain and is somewhat like the paresthesia felt in an amputated limb and referred to the portion amputated. It is possible that the paresthesia of the face is caused by functional disturbance of the central fibers of the trigeminus passing to the cerebrum.

Neither Dr. Frazier nor I would claim more for the operation of resection of the sensory root of the trigeminus than is justified by the results of one successful case, and we recognize fully that the testimony and experience of others are needed concerning the advisability of this operation. We feel, however, that one successful case is not to be ignored, and we hope that others may be induced to employ the division of the sensory root for the relief of tic douloureux.

NOTE—

I was present on October 16, 1902, when Dr. W. W. Keen exsected a portion of the roots of the Gasserian ganglion in another case. Neither he nor any of the others present, including Dr. Frazier, was able to identify the motor root as distinguished from the sensory. Dr. Keen expressed the opinion that from the operative point of view it was a much less difficult operation than avulsion of the ganglion, chiefly because of the lessening hemorrhage which left the operative field much more free.

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ACUTE ALCOHOLIC MULTIPLE NEURITIS WITH PECULIAR CHANGES IN THE GASSERION GANGLIA.*

By

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and

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The case presented in this paper is interesting on account of the occurrence of palsy of the bladder and rectum, peculiar changes in the Gasserian ganglion, and the degeneration of the nerves going to the pelvic viscera. The patient's history is as follows:

Mrs. B. K., aet. 37, was admitted to the Philadelphia Hospital on January 11, 1901 Her family and previous personal history was negative except that she had been a heavy drinker for years. The patient's history is as follows: One week before admission to the hospital she began to have pains and numbness in the extremities, muscular tenderness and weakness.

Examination. She was a fat, flabby woman with a flushed and bloated face. Her lips and teeth were covered with dried blood. She was dull and stupid. She was able to answer simple questions, but could not give any coherent account of her illness. The muscles of the legs were soft and there was great loss of power, but she was still able to flex and extend the feet, also the knees, to a slight extent, and to move the hips a little. Later there was almost complete loss of power in both legs with marked foot drop. There was complete extensor and quite marked flexor palsy of both forearms. The upper arm movements were also weak. At first she had control of both bladder and rectum, but about a week after admission both became paralyzed. There were no cranial nerve palsies. All the deep reflexes were absent. The nerve trunks and the muscles of the arms and legs were very sensitive to pressure. Tactile sensibility appeared to be normal, but hot and cold were often confused. She lost flesh rapidly not only from general emaciation, but also from local atrophy in the arms and legs. She was delirious or stupid the greater part of the time, but was mentally clear at intervals. A slight grade of jaundice developed toward the end. There was continuous slight fever averaging between 99° and 100° and twice rising to 102°for one night. The pulse rate ranged from 100 to 130; the respiratory varied from 26 to 40 per minute. For several weeks before death she had great difficulty in breathing without there being any physical signs to account for it. On February 13, 1901, her temperature fell to 97°, and she died, the radial pulse ceased to be felt some time before death.

The autopsy revealed cirrhosis of the liver; slight fatty degeneration of the kidneys and slight general arteriosclerosis. The other viscera, including the lungs were normal. Microscopic examination of the peripheral nerves by the osmic acid fresh method revealed parenchymatous degeneration of the vagus, median, ulnar, peroneal and phrenic nerves, the vesical and sacral plexuses and the corresponding anterior and posterior spinal roots. Staining confirmed the presence of this degeneration and also revealed in the vagus and phrenic hemmorrhagic extravasations between the nerve bundles and within the sheaths. Examination by the Marchi and Weigert method showed that the degeneration became markedly lessened as the central ends of the nerves were approached. The intramuscular nerve filaments were extremely degenerated and the muscle fibres by the Marchi method showed local areas of degeneration. The rest of the muscle structure surrounding these areas was unaffected.

The central nervous system studied by the Nissl, Weigert and Marchi methods and treated with the nuclear and other stains showed marked alterations. Widespread and intense chromatolysis with at times vacuolization was present in the anterior horn cells, the cells of Clarke's columns and those of the bulbar nuclei. There was intense congestion of the gray matter throughout the entire cord and medulla. The Marchi method showed intense acute degeneration of the posterior columns, the direct cerebellar tract, and to a lesser degree throughout the entire cord. The anterior and posterior roots, both intra and extra medullary, were markedly degenerated. The Weigert and carmine stains confirmed these changes and revealed an old and quite extensive perivascular sclerosis affecting the posterior and lateral tracts, (see fig. 1), presenting the appearance somewhat of a postero-lateral sclerosis (combined system disease).

The Gasserian ganglion was markedly altered. The nerve fibres were degenerated like the other peripheral nerve and nerve roots. The ganglion cells were in a condition of almost complete chromatolysis,vacuolated and very many of them completely destroyed and infiltrated with a calcareous material staining a deep purple with haem-alum and presenting a peculiar semicrystalline structure. These areas were still surrounded by the cell capsule and presented a totally different picture to other areas of infiltration of a similar nature in the neighborhood of the smaller vessels. Such areas were small in size, and bunched in the form of rosettes about the vessels. At no time did they show the peculiar concentric arrangement of the concentric bodies found in the aged and in tic douloureux (Spiller-Barker).[1] The vessels of the ganglion and elsewhere revealed evidence of an active pathological process in the thickening of the media and a marked increase of the number and size of the nuclei of the vessel walls. The most marked and striking changes were found in the cell capsules and in the interstitial tissue. There was a very marked round cell infiltration in the stroma of the ganglion without any special congestion of the ganglion. These cells were not leukocytes nor were they the small round cells found in inflammatory conditions, but were of larger size and more the shape and size of the connective tissue of the stroma. In the normal ganglion the ganglion cells are each surrounded by a capsule composed of a single layer of endothelial cells. In this ganglion the cells of the capsules had proliferated to such an extent as to form several layers about the cell and at times to completely fill the cell capsule, although this did not frequently occur, (see fig. 2). The only other condition in which these changes occur with any degree of constancy is hydrophobia. In the capsular changes of hydrophobia, however, the original layer of capsule cells is preserved, the proliferation occurring internally toward the centre of the cell, whereas in this specimen the proliferation occur both internally and externally to the capsule with complete obliteration of the original layer of capsular cells. The new formed cells are very different from those found in hydrophobia; here we find the cells with a distinct cell body and forming laminated layers of cells around the cell like so many connective cells. Such a condition of these cells is rare in hydrophobia, where we usually find but little tendency to form a spindle cell body and merely nuclei to indicate the cell proliferation. These changes together with the calcification of the ganglion cells has led us to the conclusion that these ganglion changes, especially the capsular changes are of a chronic or at least of a very subacute character with possibly an acute exaccerbation towards the end of the disease.

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*From the William Pepper Clinical Laboratory, Phoebe A. Hearst Foundation.

**Read before the American Neurological Ass'n, Boston. June 20, 1901.

[1] Spiller—Jn'l Am. Med. Assn, 1900, P. 1094.
Barker—Jn,l Am. Med. Ass'n, May 5, 1900, P. 1093.

To sum up we have a case of acute alcoholic multiple neuritis, with involvement of the bladder and rectum and acute widespread degeneration of the central and peripheral nervous systems, of the pelvic nerves, the vagus, and phrenic with hemorrhagic extravasation within the sheaths of the latter: degeneration of both fibre and cellular structure of the Gasserian ganglion (the other intervertebral and cerebral nerve ganglia not being examined) and intra and extra capsular round cell infiltration and proliferation about the ganglion cells which were in an advanced state of chromatolysis.

The changes in the Gasserian ganglia may be of some clinical and pathological significance and importance. Van Gehuchten and Nélis[2] in an article on rabies ascribed the paralysis to changes found in the intervertebral ganglia, which often were not as intense as the changes found in the ganglia here described. They came to this conclusion because no degeneration was found in the motor fibres from the cortex to the muscles and did not sufficiently take into consideration the cell changes of the spinal cord at times occurring in rabies. In any event it will be worth our while even with the presence of degeneration of the nerves sufficiently intense to cause the symptoms in alcoholic palsies, to bear in mind the possibility of these gangliar changes as a contributory factor in the production of the spinal and cranial nerve palsies. The capsular lesions in the ganglia are in all probability due to the irritant effect of the alcoholic or some metabolic poison, just as the lesions in rabies are due to an irritant product acting on these structures. Proliferation of the capsular cells has been described only two or three times outside of rabies[3] in which it constantly occurs in advanced cases. In an article on this subject one of us in conjunction with Dr. Ravenel predicted, that such capsular changes would be found in diseases due to irritant toxins, but were unable to find them in an extensive investigation of tetanus and diphtheria. Crocq[4] found in one case of fatal diphtheria, lesions analagous to rabies but differing both from that affection and the lesions described in this paper.

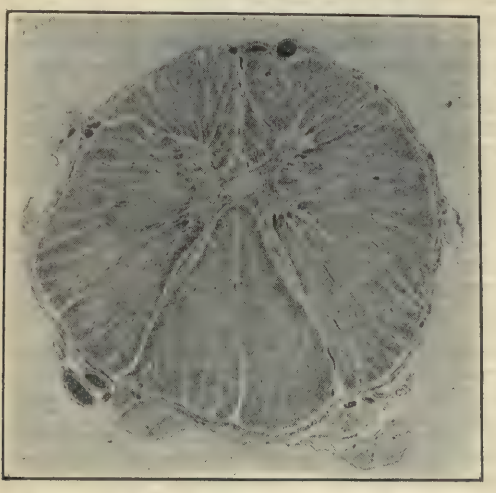

FIG. 1.—Spinal Cord of Case 1, showing degeneration in the posterior and lateral tracts; also a very marked perivascular sclerosis stained by Weigert's method; the intense congestion of gray matter is well shown, as are also the lighter colored areas indicating the degenerative portion of the cord. The white streaks are areas of sclerosis surrounding small distended thickened capillaries.

The bladder and rectal disturbances in alcoholic multiple neuritis are interesting, because it is usually taught, that they do not occur and that their presence is a differential point against multiple neuritis.[5] Oppenheim states that, in the absence of delirium or unconsciousness, it should suggest some complications such as an involvement of the spinal cord." Pathological changes acute and chronic were present in this case. The acute changes, an extension of the peripheral changes to the spinal cord, are not infrequently found in a multiple neuritis unassociated with bladder or rectal symptoms. There was no palsy of the bladder and rectum until the development of the acute disease notwithstanding the chronic sclerosis. We are therefore of the opinion that, in the absence of any special lesions in the lumbar enlargement, the bladder and rectal incontinence was due to lesion of the peripheral neuron as manifested by the intense degeneration of the pelvic nerves and sacral roots.

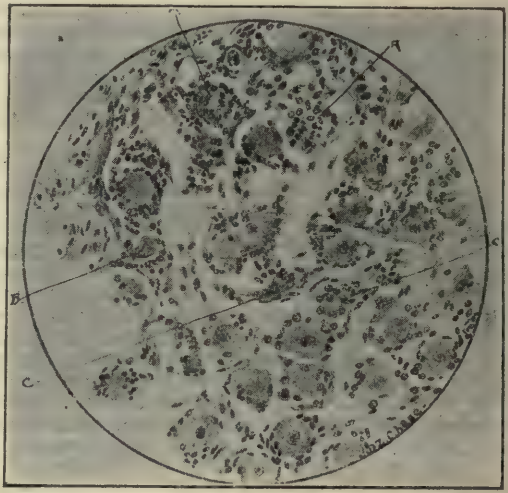

FIG. 2.—Gasserian Ganglion of Case I (alcoholic multiple neuritis) showing interstitial and pericellular and intra-capsular small round cell infiltration.

A. Capsule entirely filled with proliferated cells.

B. Nerve cell almost completely degenerated; the nucleus has disappeared and the cell is shrunken.

C. Proliferated stroma cells.

From these findings it can be easily understood why impotence is met with in some cases and amenorrhea in others.[6] It is also demonstrated in this case that a multiple neuritis with demonstrable lesions affecting the bladder and rectal nerves can occur, and too much stress should not be laid on this point in differential diagnosis from cord disease.

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[2] Van Gehuchten and Nélis Bull. de l'Acad. Royal de Méd. de Begique, 4 Serie 14, 1900.

[3] Ravenel and McCarthy—Univ. Med. Mag., Jan. 1901.

[4] Idem.

[5] Oppenheim's Lehrbuch, Zw. Aufl. '98.

[6] Buzzard quoted by Oppenheim's Lehrbuch.

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January, 1902.

CEREBRAL LESIONS IN EXPERIMENTAL LEAD INTOXICATION.

By Dr. D. J. McCarthy,

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(From the William Pepper Laboratory of Clinical Medicine, Phoebe A. Hearst Foundation.)

In the course of a series of experimental investigations on the lower animals, conducted by Dr. C. Y. White and Dr. William Pepper, (Am. Jour. Med. Sc., 1901), with a view of studying the blood changes, one of the first dogs experimented on manifested cerebral symptoms from the lead intoxication. This led to a study of the central nervous system of this dog and the others used in this series. In all, twelve brains were studied. In only one of these was the intoxication prolonged beyond one month. In several of the dogs, lead was administered during ten to twelve days. The detailed dosage will be given only in the first case, inasmuch as the lesions and their manifestations were most marked in this case, and differed from the other cases only in degree. The dosage of the lead in all the cases was practically the same, and in a general way followed that about to be described in the dog which developed the convulsions. The reason the other dogs were not kept upon the lead any length of time was due to the fact that manifestations in the blood occurred very early after the first dosage, and it was not necessary to delay the work as in the first case.

The lead was administered in the form of the acetate of lead. Grams 1.5 were placed in a capsule and given by mouth. On January 4 and 5, one capsule was given. This was increased on the fifth to 5 grams, and continued until February 28, when the dog died. On February 24 the dog had a convulsion in his cage. This attack was not carefully studied, but was a general convulsion lasting several minutes. On the following day while the dog was walking across the laboratory floor he suddenly staggered and fell to the floor in a general clonic convulsion. There was no tonic stage as in epileptic attacks. These clonic movements lasted several minutes; the dog appeared to be unconscious and was dazed for some time after the movements had disappeared. The dog died February 28.

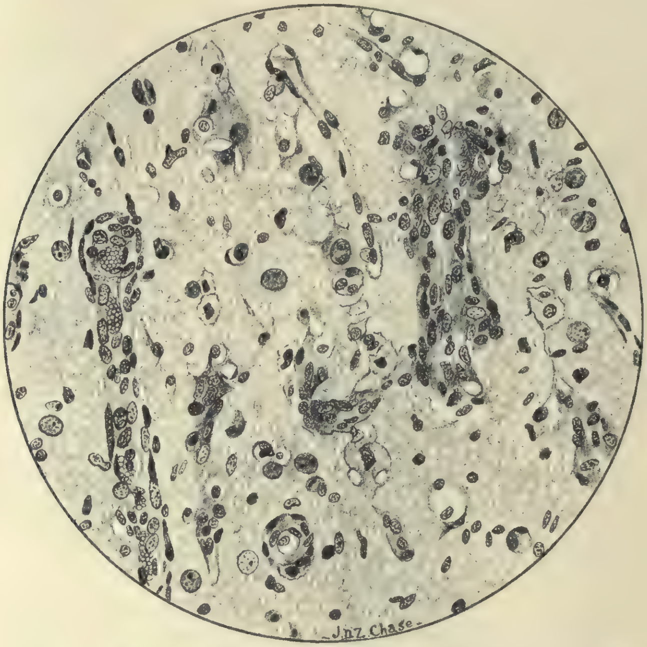

FIG. 1.—Section through the pyramidal layer of motor cortex of dog No. 1. The vascular proliferation, increase in neurogliar cells and vacuolation of the ganglion cells are shown.

At the autopsy no lesions were observed on macroscopic examination. Under the microscope the lesions were very marked and mainly confined to the cerebral cortex, and especially to that of the cortex around the gyrus cruciatus, corresponding in man to the motor area. Thin sections stained with hematoxyln and eosin and examined under a high power, presented a fine cribriform appearance. On closer examination this was found to be due to a marked degeneration of the ganglion cells followed by vacuolation. This was not the usual vacuolation met with in which there are several small vacuoles in the cell body, or one small vacuole, but consisted in a small area of cell substance taking the stain and the rest of the cell body remaining as a distended globule. These results confirmed by staining the sections with the Nissl method, which brings out so beautifully the cell structure. The only portion of the cell staining by the methylene blue was the apical extremity of the cell, the rest of the cell remaining transparent.

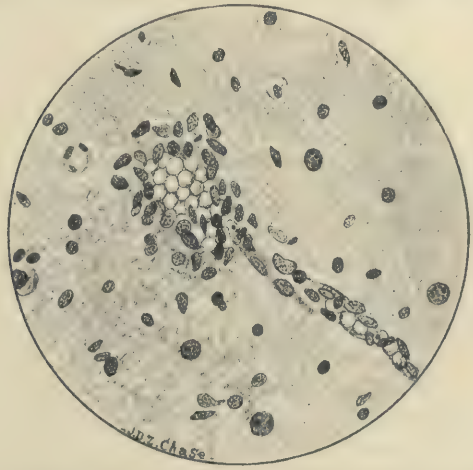

Fig. 2.—Capillary from the motor area of brain of dog No. 1. The cell proliferation of the cells of the capillary wall and the neurogliar cells is seen about the vessel.

Even more striking than the cell changes were the changes in the cortical and subcortical capillaries. The capillaries were very remarkably proliferated and completely dominated the microscopic picture. Not only was this due to the number of the capillaries in a single field, but also to the very marked thickening of the vessel walls. Even the smaller capillaries when examined in cross section were surrounded by a wall of three or four layers of cells. In the vessels of larger diameter this accumulation of cells was even more marked. A reference to Fig. 1 will give a better idea of the changes than any verbal description. Small hemorrhages were also noted in the cortex. These accumulations of free red corpuscles were never extensive, but were quite numerous throughout the sections. The proliferation of the capillaries and the thickening of the walls were also present in the subcortical tissues.

The above description represents the findings in a dog taking large amounts of lead acetate over a period of two months, and dying as a result of the intoxication. In none of the other animals were symptoms referable to the nervous system noted. All of them were killed within a month after beginning the experiment, and most of them in between two and three weeks. In the latter animals only slight changes were noted, and consisted mainly in an accumulation of cells along the walls of the radiating subcortical vessels. They were also observed in the cortical vessels, but could not be so plainly seen on account of the gliar nuclei and the ganglion cells. The degeneration of the ganglion cells was not present in these sections. In the sections of the animals dying between the second and third weeks the changes were more marked, but nowhere near so intense as in the dog showing the cerebral symptoms. Chromatolysis was present in these sections, but the capillary hemorrhages were absent.

There are several interesting points in connection with these microscopic lesions. The thickened vessel walls can best be studied in the earlier changes. In dogs killed in the second and third weeks the nuclei of the capillary walls are more frequent in number and of a more circular shape than normal. In more advanced changes there is added to this change an accumulation of gliar nuclei along the course of the vessels; this is best seen in longitudinal sections of the vessels, and is most marked in the subcortical tissues. In the motor areas of the dog first described, the most advanced changes can be studied. In cross section several layers of elongated nuclei are somewhat concentrically arranged around the lumen of the vessel; there is next a layer of cells with a more rounded nuclei, and gradually merging into the brain substance enlarged gliar nuclei in considerable numbers. (See Fig. 2.)

The degenerating cortical ganglia cells are surrounded by an accumulation of smaller neurogliar nuclei, which gradually encroach upon the area of the disappearing cell until in advanced stages no trace of the cell remains except the accumulation of small round nuclei. These nuclei are much smaller than a large vesicular nucleus frequently met with in these sections, and evidently enlarged neurogliar nuclei. There appears to be an active proliferation of the capillaries in this case. A capillary cul-de-sac can be seen reaching out to an isolated nucleus; the nuclear stain can be followed as an elongated line of chromatic material back along the border of this cul-de-sac to the next nucleus. The terminal nucleus being of an oval shape, this arrangement of the chromatin gives it a tailed appearance.

We have therefore presented to us in this series of sections a progressive degeneration with disappearance of the ganglion cells, followed by an increase in the gliar elements and associated with a very remarkable non-inflammatory endarteritis and periarteritis. The reaction of the tissues in this case to an invading toxic irritant are very marked, and associated with the capillary hemorrhages would, in that sense, constitute an inflammatory process, but I prefer not to use this term in the absence of a round-cell infiltrate other than that of a proliferation of the gliar nuclei.

This same process occurring in a human being could give all the symptoms, including the convulsions, of a case of paresis, and it can be easily understood why some cases of progressive chronic lead intoxication present the clinical picture of general paralysis of the insane. (*Oppenheim-Lehrbuch der Nervenkrankheiten.* Zw. Auf. Pp. 383). We have here the same gradual loss of active functionating brain cortex which leads to the psychical and mental deterioration in general paralysis.

We have very little, if any, positive knowledge of the mechanism on the production of the epileptic attack, but the lesions present in this one case are consistent with those present in some cases of epilepsy. The only resemblance the attacks in this dog had to true epilepsy was the apparent unconsciousness, which could not be proven, and the presence of clonic movements. Whether the convulsive tendency was due to the direct action of the toxin on the nerve cells, or was secondary to the cell degeneration, or the vessel changes or the irritation of the capillary changes, could not definitely be determined. These convulsions could not have been primary, because they occurred late in the disease, and were probably the result of the combined vessel and cell changes.

Vacuolation of the cell due to the action of lead is well known. I have been unable to find any reference to experimental findings in the cerebral capillary system in lead.

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MELANOSIS OF THE CEREBRO-SPINAL MENINGES.

By D. J. McCarthy, M.D.,

and

Mazÿck P. Ravenel, M.D.

From the William Pepper Laboratory of Clinical Medicine (Phoebe A. Hearst Foundation) and the Laboratory of the State Live-stock Sanitary Board of Pennsylvania.

We wish to present in this paper some remarks on the subject of excessive deposition of melanin pigments in the cerebral and spinal meninges based on a careful study of two cases, one a cow in which the pigmentation was extreme, and the other a human being in which the pigmentation was slight.

Case I.—The brain and upper portion of the spinal cord of a cow supposed to have died of rabies was sent to the laboratory of the State Live-stock Sanitary Board for the purpose of obtaining a diagnosis. The clinical history was strongly suggestive of rabies following the bite of a dog, and as the physician who made the post-mortem examination wounded his hand while removing the brain a positive diagnosis was important. The clinical diagnosis was confirmed by examination of the intervertebral ganglia (Fig. 1), of which more will be said later, and also by the subdural inoculation of rabbits.

On macroscopical examination the brain and spinal cord were found to be almost black, the color being most intense over the spinal cord, and gradually fading as the vertex of the brain was reached. (Fig. 2.) It was, however, very distinct over the parietal region, and to a lesser degree over the temporosphenoidal and occipital regions of the brain. The inner surface of the dura, the arachnoid and the pia were all involved in the pigmentation. There was perhaps more pigment in the pia than in the arachnoid or dura, though there was but little difference in the degree of color produced. On cross-section of the cord or brain substance it appeared as if there were an infiltration of the pigment into these tissues. The velum interpositum and choroid plexus of the fourth ventricle were deeply pigmented.

In making the microscopical examination of this case sections of the cord with the membranes intact were cut and examined, both stained and unstained.

Pieces of the pia and arachnoid were also separated from the brain and cord, spread out on a slide and mounted in glycerin without staining. Other portions were stained with hæmatoxylin and eosin or carmine, and mounted in the usual manner. The relative deposits of pigment were best seen in the unstained sections. The cellular structures and the relation of the pigment areas to the bloodvessels were best studied in the stained preparations. (Fig. 3.)

The pigment was found: (*a*) In amorphous masses in irregular-shaped cells surrounding the vessels and to a lesser degree at a distance from them; and (*b*) as a very granular matter scattered uniformly throughout the tissues and filling up the endothelial cells of the membranes. The cells of irregular conformation were completely outlined by the pigment even in the unstained sections. In some of these cells where the pigmentation was less intense it was found that the coloration was produced by a very close massing of fine granules similar to those observed in the endothelial cells. The relation of these deeply pigmented cells to the pial vessels gave the very striking effect in the unstained sections of bloodvessels with black walls. The examination of the velum interpositum and choroid plexus gave practically the same result as observed in the pia just described. In the sections in which the spinal cord and its membranes can be studied together a deep brownish pigmentation can be followed deep into the cord along the course of the bloodvessels. The pigment appears to be deposited in the cells of vessel walls. Not only in these cells, but also in the pia the pigmentation of the connective-tissue cells is very intense in the cell body, but the nucleus is left free. In some cases, however, the nucleus is not visible.

Microchemical reactions for iron were tried, but with negative results. As there was a possibility that this pigmentation might have been the remains of an old hemorrhagic extravasation, the negative reactions to the free iron tests left little doubt as to the nature of the pigment. Melanin in very small amounts is found in the pia of the cervical region of the spinal cord in human beings, and in somewhat larger quantity in the lower animals. It is very probable, therefore, that the intense pigmentation in this case was merely an accentuation of the slight pigmentation usually found in the cervical pia, in general so slight as to be inappreciable to the naked eye, though in this animal so markedly increased as to give a black color to almost the entire central nervous system. The only other change discovered in this specimen was a considerable thickening in the walls of the spinal vessels. We were, however, unable to trace any connection between this endarteritis and the pigmentation of the membranes. We were also unable to determine the cause of the arterial disease. The diagnosis of hydrophobia was confirmed by the perivascular round-cell infiltration, the pericellular infiltration, and the capillary hemorrhages in the medulla, and also by the changes found in the ganglion cells of the intervertebral ganglia. These consisted of advanced degeneration and marked vacuolation, with abundant proliferation of the endothelial cells of the capsule, as described by Van Gehuchten and Nélis. We have never met with a case in which vacuolation of the ganglion cells was more marked. (Fig. 3.)

The pigmentation was of long standing, and of course had nothing to do with the acute rabic process. In a series of more than sixty cases of rabies in various animals this is the only one showing a melanosis of a degree sufficient to make it appreciable to the naked eye.

Case II.—The second case we wish to record is that of a deaf-mute who died from tuberculosis. At the autopsy, in addition to an atrophic process affecting the left side of the brain in the occipital and parietal regions, there was a considerable degree of pigmentation of the pia and arachnoid over the pons and medulla, giving to this part of the brain a distinctly darker hue than the rest, but nowhere was it nearly so intense as in the case above described. The microscopical examination gave practically the same results as in the first case, with the exception that the pigment, instead of appearing black by transmitted light, took a reddish-brown hue. The pigment was composed of the same fine granules, but they were fewer in number and not so densly aggregated in the cells. The pigment-bearing cells were not so closely arranged about the vessels as in the first case.

Both these cases are examples of excessive deposit of pigment in tissues in which it is found normally in small amounts. In neither of them had the pigmentation any relation to the pathological process causing the death of the individual. In the cow the peculiar arrangement of the pigment and of the pigment cells about the walls of the vessels, and the presence of pigment in the walls of the vessels within the spinal cord, would support the teaching of Krukenberg that the melanotic pigments are derived from the oxyhæmoglobin of the blood by the action of light and the alkaline reaction of living tissues. In a peculiar pigmentation of nerve cells observed in a rabbit poisoned by rattlesnake venom, reported by one of the authors,[1] after a careful study of the subject we arrived at the conclusion that it was due to the metabolic action of the tissues on the hæmoglobin of the degenerated blood. In neither of these cases had the action of light anything to do with the result. We can therefore agree with Krukenberg[2] in so far that the pigmentation was the result of the metabolic action of the tissues on the hæmoglobin pigments. After blood extravasation into different tissues there is found a brownish or black pigment, giving a negative reaction for iron, and spoken of as melanin, due to the same cause. It is very probable that there are several different pigments of varying chemical composition described under the general name of melanin. Some of the melanotic pigments found in pathological tissues, such as the melanosarcomata, will give distinct iron reaction. (Nencki,[3] Lieber, Abel,[4] Dands, Schmiedeberg,[5] etc.) Schmiedeberg finds besides this iron reaction a varying percentage of sulphur and nitrogen depending upon different stages of albumin degeneration.

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[1] Contributions from the William Pepper Laboratory of Clinical Medicine.

[2] Krukenberg Grundzüge der Vergl. Physiol. der Farbstoffe u. d. Farben. Heidelberg, 1887.

[3] v. Nencki. Correspbl. f. Schweizer Aerzte, 1890, vol. xx. Archiv f. Exp. Path., 1886, vol. xx.; 1888, vol. xxiv.

[4] Abel. Virchow's Archiv, 1890, Bd. cxx.

[5] Schmiedeberg. Archiv f. Exp. Path., 1897, Bd. xxxix.

[illegible]

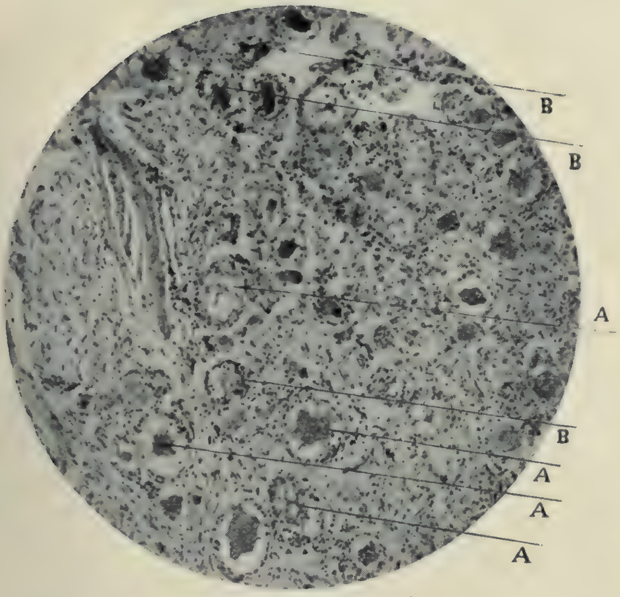

Fig. 1.—Intervertebral Ganglion of Cow (Case I.).

A. Advanced chromatolysis of the ganglion cells, with proliferation of the cells of the capsules. *B*. Advanced thickening of the capsules, with disappearance of the ganglion cells.

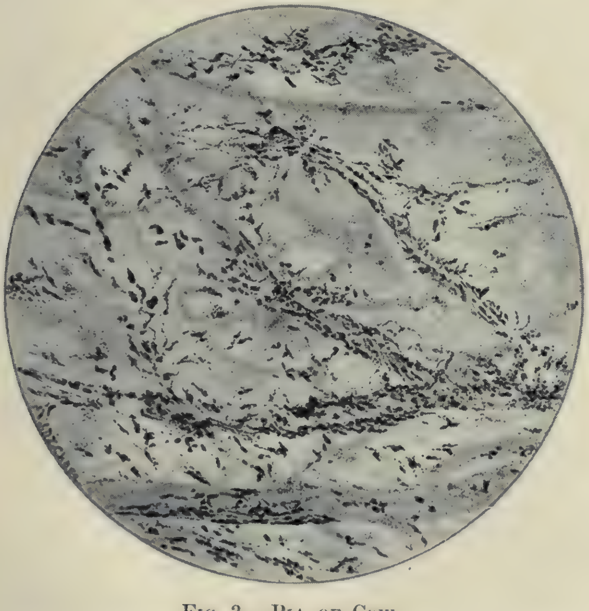

Fig. 3.—Pia of Cow.

Stained by eosin and flattened out on slide and mounted in balsam. The arrangement of the pigment cells around the vessels, outlining their course, is shown.

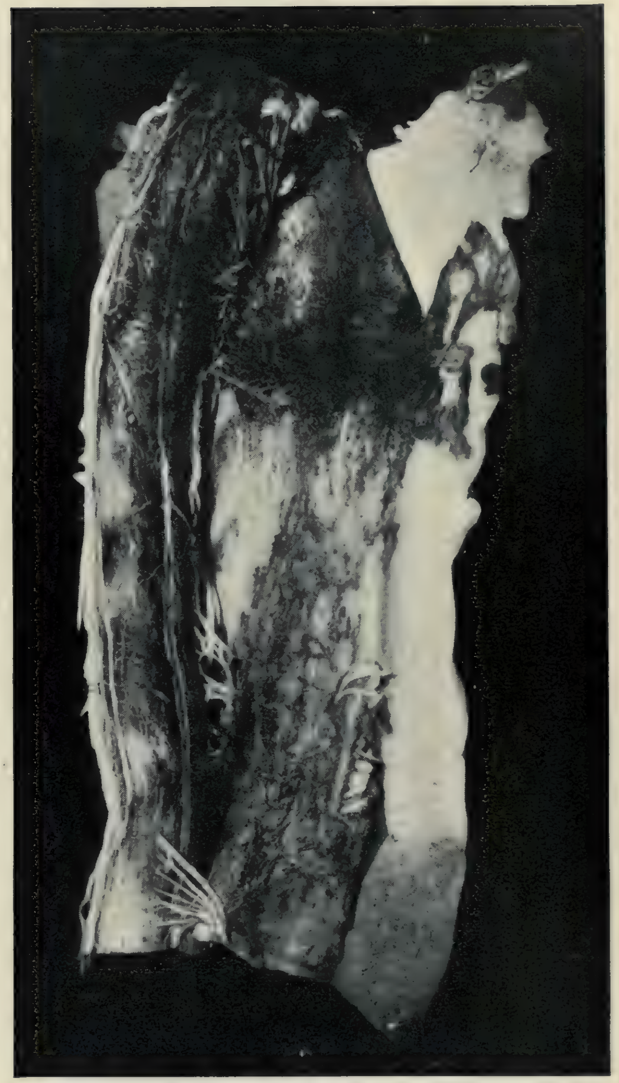

Fig. 2.—Spinal Cord of the Cow (Case I.).

The spinal cord, very deeply pigmented, is seen to the left. The dura is detached and spread out from the cord to the right of the photograph, and also shows deep pigmentation. The white area at the right upper corner of the photograph is caused by removal of a portion of the pigmented layer for microscopical investigation. The white nerve roots coming off the spinal cord at the bottom of the picture and penetrating the dura is the color which the normal cord exhibits normally.

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A CONTRIBUTION CONCERNING CREATININ EXCRETION.

BY DAVID L. EDSALL, M.D.

(*From the William Pepper Laboratory of Clinical Medicine, Phœbe A. Hearst Foundation.*)

This report is based upon the results which I obtained in estimating the creatinin excreted in the urine in a case of family periodic paralysis under the care of Dr. John K. Mitchell. The reasons for estimating the creatinin were partly the clinical nature of the case and partly as follows: I was asked to determine whether or not there was any evidence of acid intoxication in the case, and consequently searched for oxybutyric acid (the crotonic-acid test), acetone, diacetic acid, and lactic acid in the urine, determined the alkalinity of the blood during an attack and in the interval, and determined the excretion of ammonia throughout a series of attacks and the corresponding intervals. The results were all negative as to any evidence of acid intoxication, but the ammonia excretion showed a remarkable reduction (down to 100 mg. or less per day) for several days preceding the attacks, and rose to about one gram with the onset of the attacks or shortly after their appearance. Since the excretion of ammonia is an index of the amount of acids being formed and excreted, and since it is probable that the muscles play a considerable part in the production of acids in the system, the condition of the ammonia excretion before the attacks suggested the possibility that there is in this disease a decided qualitative or quantitative change in muscle metabolism which precedes the attacks and perhaps causes them. There is also the possibility that the excretion of ammonia was reduced because that of other alkalies was increased. This possibility is compatible, however, with the view that the low ammonia excretion was an index of alteration in muscle chemistry, for the excretion of potassium in particular is largely influenced by the condition of the muscles. The most satisfactory way of determining whether there were decided alterations in the chemical activity of the muscles at the times when the ammonia excretion was low seemed to be the determination of the creatinin excretion, for so far as our present knowledge of creatinin excretion reaches it indicates that it varies chiefly in relation to the condition of the muscles, excluding those variations which are due purely to diet. Creatin, from which creatinin is formed, is found in small amounts in various tissues, but is probably produced in notable amounts only by the muscles and the thyroid gland, and by the muscles in far greater amounts than by the thyroid gland. Creatin is found in very large relative quantities in the muscles, and the amount is greater if the muscle has recently been functionating actively. Further, active muscular exercise increases the excretion of creatinin. (There is some contention over this point, but I believe that the more recent work by better methods justifies this statement.) Extensive muscular paralysis and other pathologic conditions associated with marked lessening of the functions of the muscles decrease the excretion, while during actual wasting of the muscles the amount is increased. It has recently been claimed by Gregor that the excretion of creatinin is a direct index of the condition of muscle metabolism. While all the facts mentioned indicate a very evident relation between the excretion of creatinin and the activity of chemical changes in the muscles, some isolated observations tend to show that creatinin excretion may vary decidedly in accordance with other changes than those in muscles, and it cannot be said that Gregor's contention is wholly justified. But it may be said that the excretion of creatinin is more nearly an index of the condition of muscle chemistry than is the excretion of any other substance, so far as known, and there can be little doubt that some part of the excretion of creatinin, at any rate, is intimately dependent upon the chemical processes occurring in muscles. It is claimed by certain authors that the creatinin excretion in the urine is wholly dependent upon the character of the food; there is, however, no reasonable support for such a view, and there is good evidence against it.

I estimated the creatinin by the Neubauer-Salkowski method, continuing the ammonia estimations throughout the attacks in which the creatinin was estimated, and also determining the total nitrogen of the urine (Kjeldahl method) as a check upon the amount of nitrogenous food being taken. The man's diet was kept uniform during the intervals, but it was impossible for him to take the usual amount of food during the attacks. This fact, however, makes little difference in interpreting the results which I report, since the main changes to which attention should be directed occurred before the attacks, at the period when he was taking the usual amount and kind of food. The excretion of ammonia showed no changes of importance, excepting as already indicated. The excretion of creatinin and nitrogen was as follows:

		Creatinin in grams.	*Nitrogen in grams.*
March	29	0.0879	18.942
"	30	0.1482	
"	31	0.0561	19.820
April	1	0.1131	13.958
"	2	0.0819	14 490
"	3	0.5599	20.677
"	4	0.8879	20.506
"	5	0.1538	20.930
"	6	0.1819	19.257
"	7	0.0749	22.242
"	8	0.0117	23.068
"	9	0.4927[1]	11.340[1]
"	10	0.0795	17.052
"	11	0.1123	21.873
"	12	0.0499	17.606
"	13	0.0936	20.888
"	14	0.2019	20.508
"	15	0.2496	18.860
"	16	0.2247	19.152
"	17	0.1053	20.124
"	18	0.0140	18.043
"	19	0.0280	18.866
"	20	0.0031	13.333
"	21	0.0210	19.025
"	22	0.3838	15.650
"	23	0.1404	18.547

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[1] The figures for April 9th are too low for both the creatinin and the nitrogen. A portion of the urine was sent to Dr. Flexner, who investigated its toxicity. My figures are for the amount of urine that I received. Reckoned for the whole amount the figures would be: creatinin, 0 68 gram; nitrogen, 14.968 grams. I used the figures given in the table because the amount sent Dr. Flexner was fresh urine, not an aliquot part, and it could not therefore be properly reckoned with the other.

During this series of estimations the attacks came on as follows: On March 31st, lasting until late in the day following (April 1st); on April 8th, lasting through April 9th, and on April 19th, lasting through April 20th. It may be seen that preceding each of these attacks, and in the first and last instances throughout the attack, the creatinin excretion, which should normally be from 0.7 to 1.4 grams, was very greatly reduced, the amounts on several occasions being so extremely small as to be almost indeterminable, and throughout these periods being strikingly small. During the second attack, and immediately after the first and third attacks, the amount rises decidedly, the quantity found after the first and second attacks approaching the normal. It is important to observe that the low figures in each instance precede the onset of the attacks by several days, and that the reduction in excretion is, therefore, not due to the attacks. The relation to the periods of paralysis is very striking. The prolonged period of freedom from paralysis between the second and third attacks and the rise in creatinin excretion during this period seem at first to show that in this instance, at least, the relation of the creatinin excretion to the attacks was not so close as the other figures would indicate. In reality, however, the conditions during this time seem to offer even stronger evidence that the relation is a close one, for with the unexpectedly early rise of the creatinin excretion came an unexpected prolongation of the period of freedom from paralysis, and it was only when the excretion had fallen again to a very low point that the paralysis came on. The interval between attacks was, except in this instance, almost regularly seven or eight days. In this instance it was thirteen days. Another interesting fact is that the rise in excretion after the third attack was comparatively slight, and lasted only a short time, and that symptoms of an approaching attack came on several days earlier than usual (on April 24th). The last estimation of creatinin was made on April 23d, and I cannot state the conditions of excretion on the 24th or subsequently.

The conclusions that may be drawn from this work are difficult to state. The close association of creatin and creatinin with muscle metabolism and the general clinical aspects of the case make it seem at first thought probable that the results obtained indicate some qualitative or quantitative disturbance of the metabolism in the muscles, more probably a qualitative change, and that there is an accumulation of normal or abnormal toxic products which finally results in an attack, a series of changes closely analogous to those observed in the uric acid in typical gout. A fact which lends some further probability to this view is Dr. Mitchell's experience that in one other case of periodic paralysis, and to some extent in this case, a potassium salt (the citrate) seemed to prevent the attacks or to lessen their severity. The muscles contain large quantities of potassium salts, which is evidence of the importance of potassium in the functionation of muscles, and the work of Biedermann, Ringer, and others has shown that potassium salts have at times a very active excitant action upon muscular contractions, even when the contractions have ceased under the influence of other inorganic salts. Loeb's recent work has demonstrated still more clearly the marked influence of potassium upon the muscles, and though it is evident that sodium, calcium, and other salts are necessary for proper muscle function, the potassium salts are peculiarly active. It is also known that in wasting of muscles and in overexertion potassium salts are lost in large amounts, while in wasting of other albuminous tissue the sodium salts suffer more markedly than the potassium.

Possibly additional evidence of the truth of the view mentioned may be found in the fact that active muscular exercise sometimes seems to postpone attacks in subjects of this disease, and in other cases to precipitate attacks. In other words, increase in muscular function has a marked influence upon the attacks. It is, of course, impossile to exclude the influence of the nervous system in the latter connection; and, indeed, if the view that muscle metabolism is at fault be correct, we must confine ourselves to the belief that it is the immediate cause of the attack, and not the primary cause of the whole condition, for there must, of course, be some disturbance antecedent to such a supposititious disturbance of muscle metabolism.

I am, however, unwilling to state that these results indicate a disturbance of muscle metabolism. I feel that it is quite possible that such a disturbance occurs in these cases, and believe that this is the readiest and apparently the most reasonable explanation of my results. But there are several possible arguments to be offered against this view. One or two objections can be disposed of quickly. In the first place, it might be thought that the reduction in the amount of creatinin or creatin-producing food had given rise to the results. Such a criticism, as I stated before, I cannot consider of importance, because the most striking reduction of creatinin excretion occurred before the attack, at a time when the man was taking normal mixed diet, and when his urinary nitrogen was maintaining the normal level. Another possibility—*i. e.*, that creatinin was present in the urine in the usual amounts, but had not separated out as crystals of creatinin-zinc-chlorid—must be thought of, since this occasionally occurs with this method for reasons that are not well known. The low figures which I obtained made me suspect this, however, and I tested the filtrate qualitatively for creatinin by Weyl's and Jaffé's methods, and obtained only a faint reaction or none at all. A slight reaction is practically always obtained when there is any complication in the use of the method, and hence this error seems to be excluded. It might also be thought that alkalinity of the urine had transformed the creatinin into creatin, and that the low results for creatinin were due to this. I tested the urine regularly, however, and found it constantly acid. The results, therefore, must be accepted as they stand, and the difficulty is only in the interpretation of their meaning.

The chief objection to the view that they indicate solely a disturbance of muscular metabolism is that this man was taking meats in moderate quantity at the times when his creatinin excretion was lowest. Hence, he should have been excreting larger quantities of creatinin than he did, unless there was general disturbance of metabolism. In other words, the figures which I obtained, while they are so small as to indicate with much probability that there was disturbance of muscle metabolism, are so exceedingly small as to indicate strongly that something unusual must have been happening to the creatin or creatinin furnished by the food—*i. e.*, that there was probably some disturbance of general metabolism also. I think, therefore, that the only conclusion justified by the results obtained is that there is a disturbance of metabolism in this disease which precedes the attacks, and which ceases with the onset of the actual attack or directly after the attack; and it seems highly probable that this disturbance of metabolism is the cause of the onset of the attacks. Since creatinin is closely related to muscular metabolism, and its excretion shows the peculiar relation that it does to the attacks, and since the disease itself in its main clinical features is one affecting the muscles so prominently, it seems probable also that the essential feature in the disturbance of metabolism that apparently causes the attacks is an alteration in the chemical processes in the muscles themselves. This latter suggestion, however, cannot be considered to be proved.

The manner in which the reduction in creatinin excretion comes about cannot be stated. Mere retention of creatinin cannot be seriously thought of, for the total amount of creatinin excreted through a period including an attack and an interval was in all instances far below the normal. The only explanations for the figures are either reduction in the amount of creatinin produced, transformation of excessive amounts of creatin or creatinin into other substances, or a combination of the latter with retention. Mere reduction in the creatinin production is not an acceptable explanation, since the figures were lower than those that should be furnished by the diet alone if the production of creatin or creatinin in the body had ceased. Hence, whether there was retention or not, it seems most probable that the alteration in metabolism apparently producing the attacks is associated with the transformation of most of the creatin or creatinin into other substances. As to the relation of creatin and creatinin to the symptoms of the disease, I think it may definitely be denied that creatin has anything to do with the production of the paralysis. Pure creatin when ingested, when administered subcutaneously, or when injected directly into muscles, is apparently harmless; and, furthermore, the muscles normally contain large amounts of creatinin. A similar statement as to any paralytic effects is, by most authors, made concerning creatinin; but this statement is based merely upon the results of ingestion or subcutaneous or intravenous administration of creatinin. The two reports which I have been able to find which deal with the direct action of creatinin upon muscles state that when used in this way creatinin produces a brief period of paralysis or profound muscle fatigue, which is followed by entirely normal conditions of the muscles without any permanent effects. So far as I have been able to determine there has been no confirmation of these reports, and they are both old. It is, therefore, impossible to draw any conclusions from them; but a further study of the effects of creatinin upon muscles will perhaps prove of importance in determining the nature of periodic paralysis. *November* 14, 1901.

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CONCERNING THE BENZOYL ESTERS OF THE URINE IN DIABETES MELLITUS, AND THE CLINICAL SIGNIFICANCE OF AN EXCESS OF GLYCURONIC ACID.

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From the William Pepper Laboratory of Clinical Medicine, Phoebe A. Hearst Foundation.

In several communications Mayer, working partly with Neuberg, has shown that glycuronic acid is a normal constituent of the urine, and that its presence may be demonstrated by the orcin reaction if the glycuronic compounds be previously broken up by heating with weak sulphuric acid. Chiefly by the aid of this reaction he has shown that glycuronic compounds are found in the urine in excess much more frequently than was formerly suspected, and an excess is present in many cases of diabetes. The main conclusion which he draws from his work is that the close chemical relation of dextrose and glycuronic acid and the conditions under which he has found the latter practically make it certain that glycuronic acid is one of the steps in the normal oxidation of sugar; and since he found glycuronic acid present in a very large proportion of cases in which there was suboxidation, he believes that he has demonstrated definitely that diabetes is due to suboxidation.

Mayer's work is very important to the clinician in drawing attention to the fact that paired glycuronic acid is actually a common constituent of the urine and in furnishing a test by means of which its presence can be readily determined. The importance of this lies in the fact that glycuronic acid itself readily reduces copper solutions, and that paired glycuronic acid—the only form in which it appears in the urine—will reduce alkaline copper solutions after active and somewhat prolonged boiling.

It had been taught earlier by certain writers—Halliburton and others—that the most common cause of doubt as to the presence or absence of sugar in the urine is the excretion of paired glycuronic compounds. The exact basis for this teaching before the appearance of the work of Mayer and Neuberg is difficult to discover; for until Neuberg's phenylhydrazin-bromide test made it possible to show the presence of comparatively small quantities with some certainty, and until Mayer's orcin test provided a simple method of demonstrating the presence of glycuronic compounds in large numbers of cases, there was no practical way of showing the correctness of Halliburton's statements, for the methods of demonstrating the presence of glycuronic compounds were very tedious. While glycuronic compounds had repeatedly been found, and it was justly suspected that the irregular reactions often obtained were due to them, the actual proof that this was frequently true had really never been furnished.

The demonstration by Mayer that the use of the orcin reaction after heating with sulphuric acid shows the presence of glycuronic compounds is, therefore, of marked importance to the clinician, because it gives him an easy method of determining that there is a reason other than the presence of sugar itself for the doubtful reaction for sugar that he obtains. If, then, the fermentation test shows the absence of sugar, and the orcin test shows the presence of considerable amounts of glycuronic acid, uncertain reactions to copper are satisfactorily explained.

One point suggested by Mayer was of interest in another relation, viz.: Rosin and v. Alfthan reported that the benzoyl esters of the urine are largely increased in diabetes, and they believe that this indicates that diabetes involves the metabolism of all the carbohydrates and not of the dextrose alone. Mayer considers this increase to be probably due to an increase in glycuronic compounds, and not, as was held by Rosin and v. Alfthan, to an increase in the unfermentable carbohydrates. Glycuronic acid does form esters with benzoyl chloride, but Mayer's explanation as to this point does not seem wholly satisfactory, as he found glycuronic acid present in excess in only about one-third of his cases of diabetes, while Rosin and v. Alfthan had demonstrated that the benzoyl esters were increased in practically all the cases of that disease that they examined, and, further, the details of the method used by Rosin and v. Alfthan were such as largely to exclude such an error.

The readiest method of determining whether an increase in benzoyl esters in diabetes is essentially due to an excess of glycuronic acid is to estimate the benzoyl esters in cases of diabetes in which there is no evidence of the presence of an excess of glycuronic acid; and, also, in cases in which glycuronic acid is evidently increased, and to see whether the increase in the benzoyl esters is correspondingly greater in the latter cases. I have estimated the benzoyl esters in three cases of diabetes in which no reaction for glycuronic acid could be obtained; in two of them levorotation was also not present, another evidence of the absence of glycuronic compounds; in the third this test was not used. In all three I found a decided increase in the benzoyl esters—in one, to 12.56 grammes in the twenty-four hours; in the second, to 13.43 grammes; in the third, to 13.88 grammes. The normal is certainly less than 5 grammes, and probably not more than 2 or 3 grammes. On the other hand, I estimated the benzoyl esters in a case of diabetes in which the sugar had disappeared from the urine under the influence of an advanced tuberculosis, and in which there was a very marked reaction for glycuronic acid, this substance evidently being present in decided excess. In this case the benzoyl esters weighed 3.81 grammes. The amount, therefore, was at the upper limit of the normal quantity, and, perhaps, above it; but was far less than in the previously mentioned cases in which an excess of glycuronic acid was not present.

These cases, therefore, show that an excess of benzoyl esters in diabetes is not always due to an excess of glycuronic acid; and that in at least some instances, and very possibly in many, the increase in benzoyl esters is due to an increase in other substances. It has been previously shown that these substances, in large part, at least, and probably almost entirely, are of the carbohydrate group. It seems highly probable, therefore, that the original statement of Rosin and v. Alfthan, that the unfermentable carbohydrates are excreted in excessive amounts in diabetes, is true. If there is excessive excretion of unfermentable carbohydrates, it is an interesting fact, since it demonstrates that the metabolic disturbance in diabetes does not involve the dextrose alone, but that there is in this disease an actual disturbance of the whole carbohydrate metabolism.

This fact is chiefly of interest and importance because it indicates that diabetes is a more complex metabolic disorder than it is commonly looked upon as being, and that the disturbance is not one that is subject to explanation by theories which consider only the destruction of dextrose; more particularly, it serves to strengthen the rapidly increasing testimony that the belief which has become so prevalent that the whole disease may be explained by the search for a glycolytic ferment and for changes in this ferment is incorrect.

The figures that I report are of some interest in connection with the question of the source of the substances forming the benzoyl esters. Rosin and v. Alfthan consider that they are elaborated in the body. I have previously reported some figures which make it seem more probable that their essential source is the food. The figures in the first three cases herein reported lead me to believe more definitely that the opinion I expressed was correct. These cases were of varying degrees of severity, but were, temporarily, with this question in view, put upon almost exactly the same diet, the amount of protein food in particular being practically the same by weight in all the cases. In spite of the fact that the dextrose excretion varied greatly in the three cases, reference to the figures will show that the esters formed by the unfermentable carbohydrates varied only between 12.56 and 13.88 grammes. In the cases reported by Rosin and v. Alfthan the esters varied between 9 and 20 grammes. Their cases were, individually, probably on diets which varied considerably. Hence, it seems probable that the amount of benzoyl esters varies directly with variations in the diet—chiefly in the protein food.

There is another side to the question of the excretion of glycuronic compounds, however, which is, perhaps, of broader interest than the one upon which I have just touched. Mayer shows that glycuronic compounds are excreted in excess in a large variety of conditions, including diabetes mellitus, typhoid fever, and other infectious diseases, conditions associated with alimentary glycosuria, severe circulatory disturbances, etc.—*i. e.*, in a general class of cases in which this author accepts the existence of suboxidation. He decides, therefore, that the presence of an excess of glycuronic compounds in the urine is an evidence of suboxidation of sugars, and that his work demonstrates definitely that diabetes is due to suboxidation. He consequently concludes that Naunyn is wrong in his theory that the disturbance in diabetes may be one in the synthesis of glycogen from sugar, rather than in the oxidation of sugar itself.

A wholly different interpretation may reasonably be placed upon Mayer's results. In all the conditions in which he shows the presence of an excess of glycuronic compounds, either there certainly was more or less marked intoxication of varied nature, or intoxication may reasonably be supposed to have existed. In diabetes intoxication is certainly present. Alimentary glycosuria ordinarily occurs in cases in which there is an intoxication of some kind, and it is probable that the cases in which Mayer tested for it, and in which he found excess of glycuronic compounds were cases in which there was intoxication. In infectious conditions there is, of course, intoxication, and there can be no reasonable doubt that there is intoxication in marked circulatory disturbance.

I have found glycuronic compounds present in excess (orcin test) in 4 of 8 cases of diabetes; in 5 of 6 cases of typhoid fever; in a number of cases of general sepsis; in severe tonsillitis, evidently accompanied with septic intoxication, and in several other infectious conditions. In all of these, as in Mayer's cases, there was much evidence of the existence of intoxication; in most of them it was certainly present.

We know that glycuronic compounds appear in the urine after the administration of various drugs which are capable of forming compounds with glycuronic acid. Under these circumstances the formation of the glycuronic compounds is evidently a method of protecting the system from poisoning, for the effect is to cause the excretion of the poisons in a form in which they are nearly or wholly innocuous. We also know that most if not all similar synthetic combinations that occur in the body have the purpose of protecting the tissues from the poisonous action of one of the substances which enter into the synthesis; for instance, glycocol and benzoic acid form hippuric acid, this combination protecting the system from the injurious effects of the benzoic acid, and a much more common and more generally known procedure of the same kind is the synthesis taking place in the formation of the conjugate sulphates of the urine. The facts which Mayer has demonstrated and the conditions under which I have found glycuronic compounds present are not really definite evidence, as he claims, that glycuronic acid is a stage in the katabolism of sugar; they are merely evidence that glycuronic compounds occur in the urine much more frequently than was thought. Indeed, the marked inconstancy of these compounds in diabetes seems rather to be evidence that their appearance has nothing directly to do with the condition of sugar metabolism—and Loewi has demonstrated experimentally that a marked increase of glycuronic compounds in phloridzin diabetes is not accompanied by a corresponding reduction in sugar excretion, as it should be were Mayer correct in his belief.

The most satisfactory explanation of the appearance of the glycuronic compounds under the conditions in which Mayer described them, and in which I have likewise found them, is that, as in the conditions in which they were previously known to occur, they are evidence of the presence of intoxication and of the efforts of the organism to overcome this intoxication. Looked at from this standpoint one must consider that their presence is of no importance in determining the nature of the metabolic disturbance in diabetes, and that Mayer's reports do not show any new facts actually concerning the course which sugar normally takes in oxidation. His work, however, does make it seem probable that the demonstration of large amounts of glycuronic compounds in the urine is a method which may frequently be successfully used to determine the existence of intoxication in conditions in which intoxication has been only suspected or has been thought to be absent. In this connection, it seems to me worth while to investigate further the fact that I have obtained a marked orcin reaction for glycuronic acid in a number of cases of hysteria, neurasthenia, and various neuroses when all evidences of gastro-intestinal disturbance were absent. One point which Mayer makes would be of much importance if true—*i. e.*, that the appearance of glycuronic compounds in the urine may be looked upon as probably indicating a condition midway between the normal state of carbohydrate metabolism and actual diabetes, and that the presence of glycuronic compounds should therefore serve as a warning of the possible development of diabetes in the individual under inspection. This may prove to be true to a limited degree, but it will almost certainly not be shown to be a general truth; indeed, it is extremely improbable that it will ever be possible to anticipate the development of diabetes in this way. Mayer himself finds glycuronic compounds to be present very frequently, while, from a comparative stand-point, diabetes rarely develops in the conditions in which these compounds are found.

Again, as was stated, it is highly probable that in the conditions in which it has been found, paired glycuronic acid indicates the presence of an intoxication, not of an impairment of the oxidation of dextrose; and, finally, it is extremely probable (Emil Fischer) that glycuronic acid (that which appears in the urine, at any rate) does not form through oxidation of dextrose and then become paired with other substances. It is probable, on the contrary, that the pairing takes place before any oxidation of the dextrose molecule occurs, and hence that alterations in oxidation have not in themselves any influence upon the quantity of glycuronic compounds found in the urine. Hence, even if diabetes is purely a disturbance of the direct oxidation of dextrose there is no good reason for believing that the appearance of glycuronic compounds indicates the subsequent onset of diabetes.

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SPECIFIC GRAVITY OF THE URINE AND NITROGEN ELIMINATION IN PREGNANCY.

By Caspar W. Miller, M.D.

From the William Pepper Laboratory of Clinical Medicine, Phoebe A. Hearst Foundation.

One of the fundamental principles of modern metabolic chemistry is the recognition of the intimate and enduring relation between ingested and eliminated nitrogen. Thus, if in an individual in nitrogen equilibrium the proteid of the diet be increased the nitrogen elimination of the following period will also be increased and in an almost quantitative sense; and in like manner, although somewhat less abruptly, a decrease in the nitrogen consumed causes a decrease in the amount eliminated. Hence it follows that a decrease in the urea or even of the total nitrogen of the urine cannot of itself be taken to prove an insufficiency of eliminating function of the kidney unless at the same time we have analytical data concerning the diet. Since, however, it is still common for obstetricians to make routine urea examinations, it occurred to the writer that it might not be without interest to find what relation exists between the specific gravity of the urine and the urea and total nitrogen, respectively, in normal cases of pregnancy, and with that object the following experiments were undertaken.

Specific gravity.	*Per cent. nitrogen.*		*Per cent. urea.*	
1008–1009 . . .	0.26 0.41 0.42 0.40	0.37 per ct.	0.56 0.76 0.86 0.80	0.75 per ct.
1010–1011 . . .	0.26 0.25 0.37	0.29 per ct.	0.53 0.39 0.71	0.54 per ct.
1012–1013 . . .	0.36 0.33 0.51 0.50 0.41 0.44	0.43 per ct.	0.73 0.64 1.05 0.97 0.78 0.80	0.83 per ct.
1014–1015 . . .	0.56 0.48 0.58 0.53 0.49 0.34 0.68 1.02 0.40	0.56 per ct.	1.05 1.02 1.15 1.07 1.02 0.6 1.34 1.90 0.70	1.10 per ct.
1016–1017 . . .	0.65 0.59 0.72 0.69 0.83 0.63 0.72 0.75 0.71 1.02 0.43	0.70 per ct.	1.15 1.10 1.34 1.34 1.55 1.24 1.34 1.47 1.18 2.01 0.86	1.33 per ct.
1018–1019 . . .	0.46 0.99 0.40 1.02 0.90 0.67 0.46 0.93 0.63	0.72 per ct.	0.88 1.88 0.72 2.20 1.69 1.31 0.88 1.74 1.15	1.38 per ct.
1020–1021 . . .	1.08 0.66 0.60	0.78 per ct.	2.30 1.26 1.17	1 58 per ct.
1022–1023 . . .	0.90 1.01 0.92 0.99 0.82	0.93 per ct.	1.68 1.85 1.74 2.01 1.61	1.78 per ct.
1024–1025 . . .	1.29 0.93 0.88 1.51 1.40 0.69 1.08 1.65	1.18 per ct.	2.29 1.37 1.77 2.77 2.68 1.33 1.98 3.28	2.18 per ct.
1026–1027 . .	1.04 1.47 1.20	1.24 per ct.	1.93 2.68 2.28	2.30 per ct.
1028–1029 . . .	1.54 0.85 1.51 1.48 1.71 1.36 1.38 1.74	1.45 per ct.	2.74 1.66 2.81 2.53 3.11 2.73 2.65 3.27	2.69 per ct.
1030	1.18		2.09	
1033	2.02		4.29	
1037	1.91		3.46	

Since they comprehend merely a physical examination of the urines, and are in no sense a clinical study, the total quantity for twenty-four hours was not taken; while, on the other hand, care was taken to choose the samples from urine voided at various times of the day. The method was as follows: The urine was filtered and tested for albumin and sugar. In case it contained either it was discarded except where the quantity of albumin was very small. The specific gravity was then taken by hydrometer, one or, if deemed necessary, two urea estimations by the hypobromite method (Marshall's apparatus), and, finally, a Kjeldahl-Argutinsky estimation (with control) of the total nitrogen. The weighing or freezing-point methods would have given greater accuracy as regards solid content, and the substitution of the Moerner-Sjoeqvist method, or even of Huefner's for Marshall's apparatus, would also suggest itself. But as it was desired to carry out the work by the methods usually employed clinically, it was thought best not to introduce any of the refinements of the laboratory. For this reason the only correction applied to the volume of the nitrogen representing the urea was for temperature, this being the most important and at the same time the only one which can conveniently be used by the clinician.

The number of specimens analyzed was seventy-two, taken from forty-one women, all in the later months of pregnancy. Where more than one specimen was taken from the same woman an interval of several days was allowed to pass. The number of experiments was not sufficiently large to permit of a continuous curve if plotted by individual numbers of the specific gravity scale, and the results are therefore compiled for each two numbers. This is, however, of little importance, since there is often difficulty in reading correctly to the fourth figure on the ordinary instruments, and the latter

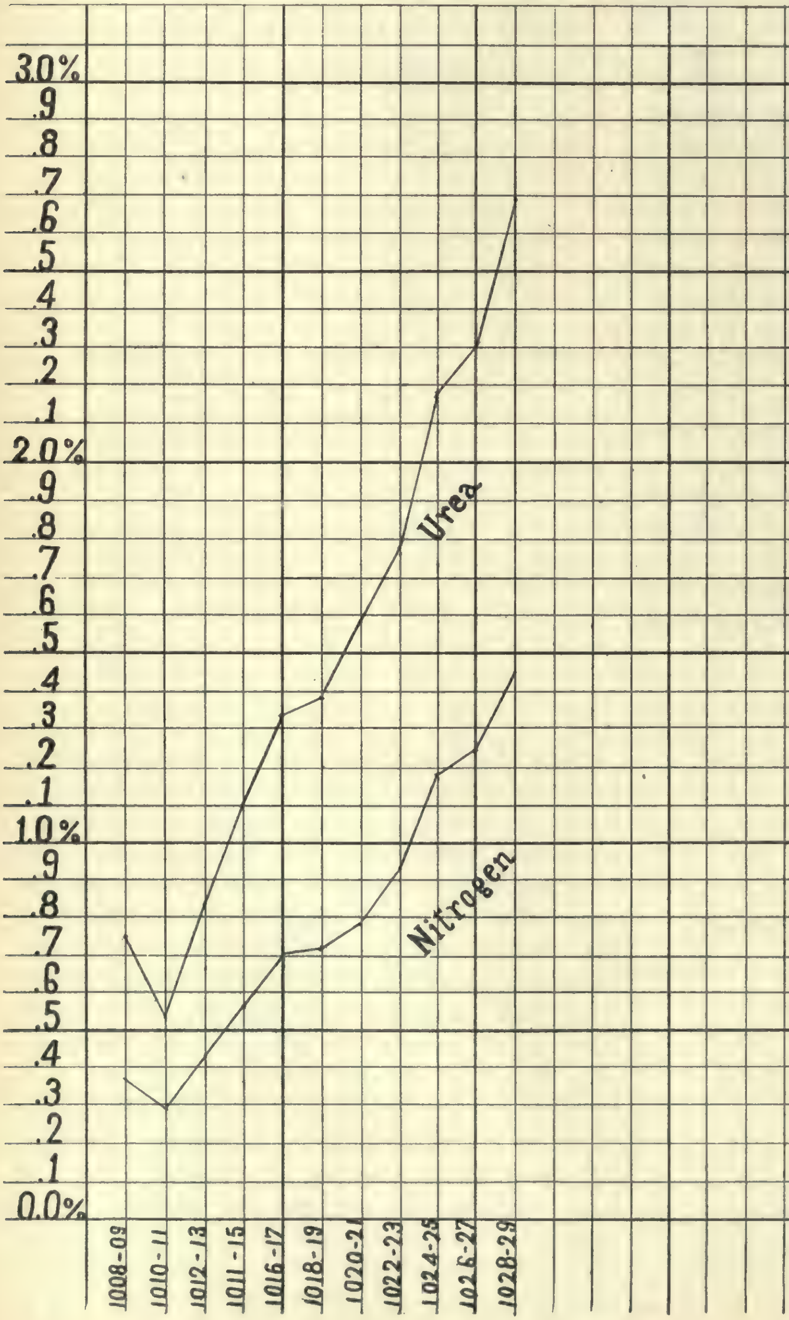

Fig. 1.

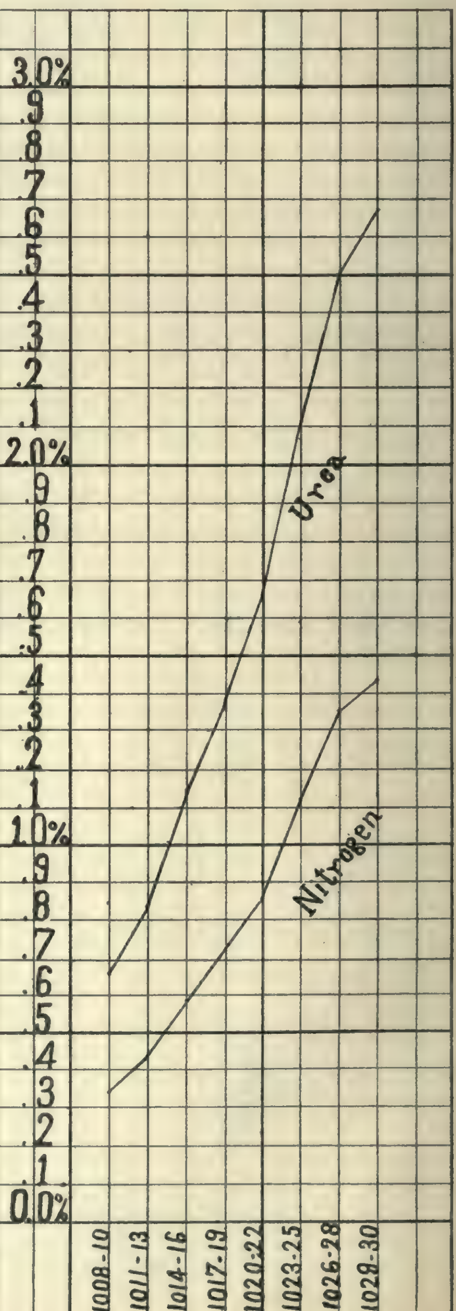

Fig. 2.

are usually inaccurate by at least this amount, particularly when no allowance for temperature is made.

The preceding table (page 1) shows the results obtained. In both urea and nitrogen analyses the calculation was carried to the third decimal place; but in the tables only two places are shown, the third figure being dropped where it is less than five, but where it is five or more one is added to the second figure.

For more convenient presentation the averages obtained from the table are shown plotted in Fig. 1. The curves so obtained, while somewhat irregular in form, show in the main a progressive increase following the increase of specific gravity. The reentrant angle for 1010-1011, as well as the other irregularities, can doubtless be explained by the small number of observations in some of the groups. That this is at least the principal reason is shown by Fig. 2, in which are plotted the averages obtained by arranging the results in groups of three specific gravity numbers instead of two, when, as will be seen, the curves become very regular.

From the results shown we are justified in concluding that: 1. There is a general and progressive increase in nitrogen and urea content accompanying an increase in specific gravity. 2. The average rate of increment is approximately 0.10 per cent. nitrogen and 0.18 per cent. urea for each increase of two specific gravity numbers. 3. The average variation in both rate of increment and individual values is, however, so large that the specific gravity can furnish only a rough indication of the probable nitrogen content.

For the material used I am indebted to the Maternity Hospital of Philadelphia, and to the kindness of Dr. Barton Cooke Hirst, of the University of Pennsylvania.

A STUDY OF THE POST-OPERATIVE CHANGES IN THE BLOOD.

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and
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The importance of an examination of the blood, as an aid to the diagnosis of surgical affections, is now fully recognized and its value to the surgical clinician fully appreciated. The statistics compiled from repeated observations have been very carefully studied and their interpretation presented to the profession, so that to-day the well-informed surgeon knows in what class of cases an analysis of the blood will render him assistance in differentiating one affection from another. From a practical standpoint three classes should be recognized: one in which a report upon the condition of the blood is of positive value. In this class should be included the inflammatory as opposed to the non-inflammatory lesions: The second, in which the blood analysis is of doubtful value, doubtful in that the results are not constant, in which category I include the malignant tumors. It has been demonstrated time and again that there may or may not be a moderate leukocytosis in patients suffering from malignant growths. Should there be a leukocytosis, it is advisable to give it due weight in the study of an obscure case, and after all, it is only in the more or less obscure cases that the clinician requires the aid of such evidence. If I might be allowed to diverge for a moment at this juncture to enter a plea for the systematic and routine examination of the blood. I have already said that it is only in the more or less obscure cases that we call to our assistance the information derived from the blood analysis, and trivial as this may appear, viewed independently of other evidence, it may prove to be the straw which throws the balance of weight in favor of this or that lesion. But in order that we may estimate at its proper value the part which blood examinations are to play, we should have at our command thousands of observations, and if every surgeon does not make it a rule in his practice to have the blood examined, as he does the urine, in every case, if he requires a blood analysis in none but his obscure cases, the statistics which we want will never be forthcoming. In my service at the University Hospital I have formulated and put into execution the following rules:

Directions for the Hemotologist.

I. Pre-Operative Records.

1. On the admission of the patient to the hospital, the following blood analysis is made: The percentage of hemoglobin, the number of the erythrocytes and leukocytes is estimated, and of the latter a differential count is made.
2. A count of the leukocytes is made at 9 a. m. on the day of the operation.

II. Post-Operative Records.

1. In all major operations, including those invading the peritoneal cavity, amputations of the extremities and breast, and the removal of large tumors, a daily estimation of the white blood cells is made until they return to normal.
2. In complicated cases, the frequency of the counts is determined by the nature and character of the complication.
3. In operations invading the peritoneal cavity, and in abdominal injuries where there is reason to suspect perforation of a viscus or serious internal hemorrhage, a leukocytic count is made at least every third hour
4. A differential count is never required except upon the patient's admission to the hospital, unless condtions arise which suggest the importance of such a record.
5. The daily blood count must be taken at as nearly as possible the same hour, and always at such a time as to avoid as far as possible the digestive leukocytosis.

Directions for the Nurses.

The following data must be observed and recorded upon the nurses' record.

1. Temperature, pulse and respirations every third hour.

2. Vomiting; quantity and character of the vomited matter.

3. Amount of urine voided in twenty-four hours.

4. Number and character of stools in twenty-four hours.

5. Diet; whether liquid, light or full diet; if liquid, the quantity of fluids ingested.

6. General condition of the patient.

7. The amount of sweating during the recovery from ether.

(The anesthetic chart contains memoranda as to the length of the operation, the amount of ether used, the general condition of the patient, etc.)

It is hardly necessary for me to lay stress upon the importance of enforcing these rules. One cannot always foresee the complications that may arise or the conditions that may develop which may subsequently render the blood analysis of importance.

Upon the patient's admission to the hospital, the diagnosis may seem to admit of no doubt, but the revelations at the operation may prove the diagnosis to have been false, and demonstrate an error which might, from the evidence of a blood examination, have been avoided. Or, to cite another example, during the post-operative period complications may arise, which suggest the possible value of a blood analysis. If up to this time no record of the blood has been taken, the value of the blood count at the first observation must be greatly discounted, since it is by a comparison of results of repeated observations that the greatest assistance is to be derived. If the surgeon has not taken the precaution to ascertain whether there was a leukocytosis previous to the onset of the complication, or, if a leukocytosis was suspected, what its degree, he will be sure to censure himself for his neglect in having lost what might have proved a golden opportunity.

To return to the point of divergence. I may cite as an illustration of the value of the blood analysis in malignant disease the differential diagnosis of sarcoma of the peritoneal glands, from tabes mesenterica. In pure tubercular infections there is, as a rule, no leukocytosis; in the presence of sarcomata there *may* be a leukocytosis—its presence furnishes positive evidence, its absence negative evidence.

The third category includes those cases in which the blood findings are difficult of interpretation, and may prove deceptive. I refer particularly to cases of an undoubted inflammatory or infectious nature where the degree of leukocytosis bears no definite ratio to the degree or extent of infection, and therefore gives no idea of the gravity of the case. Several drops of pus pent up in the tip of the finger may cause a leukocytosis double or treble that of an acute cholecystitis or a perforative appendicitis.

Other investigations of which the surgeon should inform himself are the blood changes induced by ether. DaCosta and Kalteyer (*Annals of Surgery*, September, 1901) present their report of a comprehensive study of the blood before and after ether, and their conclusions contain points of practical importance, chief among which is the danger attending the administration of an anesthetic to patients whose hemoglobin has been estimated at or below 50 per cent.

Investigations have been made also of the blood state following hemorrhage and shock.

The observations which are recorded in this paper deal only with the condition of the blood in the post-operative period, and are confined therefore to a phase of this subject which has hitherto not been dealt with. The statistics which have been arranged in tabular form, include the records in every case of an estimation of the hemoglobin, of the number and condition of the erythrocytes, and finally a record of the differential leukocytic count. The results of these investigations have been given accurate expression in figures, and these, together with the technique adopted, will be found below in Dr. Holloway's contribution to the paper, which represents an immense amount of work. In order to eliminate the error of personal equation, Dr. Holloway examined the blood himself in every case below reported, and he should be accredited with whatever value or importance may be attached to the conclusions to which we have arrived.

I. *Hemoglobin.*—I have not been able to discover in the figures at my command an alteration in the percentage of hemoglobin that is of any practical significance. Cabot has called attention to the fact that regeneration of blood after operation for malignant disease takes place in a normal manner, in refutation of Beerfreund's statement to the contrary, but this is a phenomenon of little if any practical significance. The results of our limited observation upon malignant cases conform with those of Cabot. I can conceive of cases in which the conditions of the hemoglobin may serve as an index of the anemia from which the patient might be suffering as a result of excessive hemorrhage, primary, intermediate or secondary, where the estimation of the hemoglobin would serve as a guide to the treatment necessary to hasten restoration of the blood to its normal quality and quantity. The estimation of the hemoglobin would furnish evidence which would point to a serious internal hemorrhage.

II. *Erythrocites.*—A very careful examination of the erythrocytes as to number, as to any irregularity in size or shape, as to any form of degeneration, failed to detect any abnormality of any significance. The count made immediately before the operation was relatively high, but as Dr. Holloway has pointed out, this is unquestionably due to such concentration of blood as would follow any course of preparatory treatment, including the withdrawal of nourishment, particularly liquids, and brisk purgation. There were factors during and after the operation which increased the concentration of the blood, as, for example, vomiting, sweating, purgation, restricted diet, etc., and were responsible for a relatively high percentage of erythrocytes. Holloway's results showed that there was a slight rise between the first (or pre-operative) and second count, and that from the second till the last count there was a gradual fall: expressed in figures the averages are as follows: First (or pre-operative) count, 5,492,000; second (immediately after operation), 5,584,000; third, 5,539,000, and last, 5,276,000.

Some value may be attached to the counts made after the operation, in so far as they demonstrate the rapidity with which the elements of the blood are regenerated after hemorrhage. If you single out certain operations in which there was a considerable though not alarming, loss of blood, you will discover that within two or three hours after the operation the number of erythrocytes was in excess of the number before the operation.

A few polychromatophilic cells were found in two instances and a normoblast once. There was a slight irregularity in a few, but basic degeneration in none.

III. *Leukocytes.*—Although as many and as careful records have been taken of the leukocytes, it is only in the latter that any significant deviations from normal have been found in our investigations during the post-operative period. These deviations will be discussed under various headings.

1. *Time Required for Return of Leukocytes to Normal.*—In uncomplicated cases the average time required for the leukocytes to return to normal was three and a-half days. This estimate does not correspond with that of Cabot, who, from a count of ten cases, places the limit at thirty-six hours, nor with the statement of Bloodgood, who writes: "On the whole, in the average operation, one should expect the leukocytes to be within the normal limits—twenty-four hours after operation." On the other hand, C. Y. White found that in a series of twenty-eight celiotomies the leukocytes returned to normal on an average of the fifth day. Cabot's figures were based on the reports of but ten cases, and no data were furnished by Bloodgood to substantiate his claim. From a careful study of the count in individual cases of this series, I am convinced that three days and a-half is a conservative estimate, and that were we to expect a return to normal in twenty-four or thirty-six hours, we would in the majority of operations be doomed to disappointment. In uncomplicated cases the time required for the return of the leukocytosis to normal seems to bear no definite relation to the degree of leukocytosis. A case with 30,000 will return to normal as soon as one with 20,000, and in all cases the drop to normal is progressive. There is this to be said, however, that the behavior of the case with the high count differs from that with the low count in the period between the first and second count. That, whereas in all cases above 25,000 the difference between the first and second count will average 10,000, in those cases below 25,000 the difference between the two counts will average approximately 2,000. From this time on the variation between these two categories will be proportionately less.

2. *The Relation the Degree of the Leukocytosis bears to the Extent or Character of the Operation.* Is there, or is there not, any relation between the two? Reasoning wholly on *a priori* grounds, we would expect to find the leukocytic count the higher after the operation, in which the wound was the more extensive, and invaded longer and deeper planes of tissue, as well as the one in which the dissection was such as to inflict greater traumatism upon the tissues. Bearing in mind the part the white cells play in the physiologic process of repair and their rôle as phagocytes in carrying off necrotic tissue, blood clots and the products of tissue metabolism elaborated in tissue repair, one would expect to find a higher leukocytosis after an amputation of the breast or a nephrotomy than after a trephining, an excision of a lipoma or the removal of an epithelioma of the lip. The leukocytes play the most conspicuous part in the earliest stage of wound repair when they fill in the dead spaces and furnish the pabulum necessary for the physiologic activity of the tissue engaged in effecting union until new blood-vessels are regenerated. Consequently, immediately after the operation we would expect to find them in greatest numbers. What I have advanced purely upon hypothetical grounds is substantiated by figures. The highest leukocytic count after four cases of trephining was respectively, 13,000, 14,000, 15,000, and 17,000; after an excision of an epithelioma of the lip, 17,000; after an operation for varicocele, 13,000. The highest leukocytic count after a nephrotomy, 32,000; after three Bassini operations, 31,000, 27,000 and 24,000, respectively, and after four uncomplicated appendectomies, 30,000, 29,000, 18,000 and 29,000. In all but the nephrotomy and the lipoma the highest count was recorded on the

day following the operation, and in the entire series only seven cases registered a higher count at a later period, namely, on the second day.

3. *Relation of Degree of Leukocytosis to the Temperature in Uncomplicated Cases.*—It has been said that traumatic fever is due to the circulation in the blood of certain products of tissue metabolism, to which Buchner gave the names alexins and sozins. No theory has been advanced to disprove this statement, and no other explanation has been offered. The results of our analysis of the blood in post-operative traumatic fever throws no additional light upon the situation. The leukocytic count bears no constant relation to the temperature, and the leukocytoses and temperature return to normal, the one independently of the other. A difference of one degree in the temperature upon successive days may be associated with a variation in the leukocytic count of from 1,000 to 10,000 or more. Whatever, therefore, may be the substances in the blood which disturb that equilibrium between heat dissipation and heat production, as manifested by traumatic or aseptic fever, they are not influenced by any alterations in the corpuscular elements of the blood or in the hemoglobin. However, the assertion may be made with perfect propriety that the same factors which cause a continuation of the fever may also cause a continuation of the leukocytosis. I recall a case of severe contusion of the buttock with the formation of a large hematoma in which the return of the temperature and blood count to normal consumed a period of ten days. The intercurrence of infection will, as we will presently see, affect simultaneously the temperature and blood count.

4. *The Behavior of the Leucocytes in Uncomplicated Cases.*—From what has already been said, it will be seen that, as a rule, irrespective of the character of the operation or of the temperature or of the degree of leukocytosis, there is a gradual but progressive and uninterrupted return to normal. The higher the leukocytosis, the more rapid its descent, the wider will be the daily variation, and, as already pointed out, the greater variation will almost invariably be found between the first and second counts after the operation. No matter whether the leukocytosis be 35,000 or 15,000, the normal percentage will be approached, if not actually reached, on or about the same day. In this phenomenon, then, we have a very valuable guide to the course the case is pursuing, and through knowledge of it we should be able to detect the presence of some condition or other which complicates the convalescent period. What, then, are those conditions, which can be held accountable for interruption of the decline of the leukocytosis, or in other words, what complications affect the leukocytosis in such a way as to cause fluctuations or make the fall more protracted or arrest the return to normal?

5. *Conditions Affecting the Progressive Fall of the Leukocytes.*—(a) Drugs. There are certain drugs which are accredited with the power of producing leukocytosis, and among these are included the opiates, quinine, antipyrin and phenacetin. Our personal experience offers no evidence which would either confirm or refute this statement.

(b) Vomiting, sweating, and brisk purgation, in fact all conditions causing concentration of the blood, will theoretically tend to increase the percentage of leukocytes. In every one of our recorded cases a note was made as to whether or no excessive vomiting occurred during the recovery from ether, but in none was the vomiting *per se* severe enough to exert any appreciable influence upon the leukocytosis.

(c) Information as to the degree of pain or restlessness was furnished with each case, but neither of these factors seemed to exert any influence over the leukocytic count.

(d) *Dressings and Removal of Drainage.*—When the wound was not closed at all, or when opened sufficient to allow of the introduction of drainage, a slight rise in the leukocytes was noted after the dressings. The removal of the packing or a drainage tube from a more or less open wound, and even irrigation, seemed sufficient to cause either a slight rise in the leukocytes or caused them to remain stationary. The explanation of this phenomenon would seem to be based upon the additional trauma inflicted upon the tissue at the time of operation, since we are well aware of the effect trauma itself plays.

(e) Ether, it is alleged, will increase the number of leukocytes, although no relation has ever been established between the amount of ether or the length of the period of anesthetization and the degree of leukocytosis. The same factors concerned in the relative increase of the number of erythrocytes by blood concentration, such as vomiting and purgation, or sweating, hot baths, withholding of food, both liquid and solid, will likewise cause a relative increase in the number of leukocytes. Inasmuch as patients about to take ether are given a preparatory course of treatment, which includes the withdrawal of fluid, and purgatives, and inasmuch as patients during and after ether anesthesia, sweat profusely and vomit frequently, they are subject to all the conditions which tend to produce blood inspissation. You will find several cases upon our records in which a cystoscopic examination was conducted under ether, and any disturbance of the white blood cells would naturally be attributed to the ether rather than the manipulation of the cystoscope; there was in each a slight rise, which of itself must be considered insignificant. Compared, however, with the frank leukocytoses with an increase of five, ten, fifteen or twenty thousand leukocytes per cu. mm. in round numbers, which we see with the greatest regularity after any of the operations tabulated in our series, the trifling elevation of the leukocytes which are said to follow etherization, sinks into comparative insignificance.

Granting ether, or the circumstances attending its administration, have a slight effect upon the leukocytes, it is only of an evanescent character, and will not disturb the behavior of the blood after the first twenty-four hours of the post-anesthetic period. Cabot, in an examination of fifty cases, after the patient was fully anesthetized, but before the operation was begun, concluded that there was little if any leukocytosis. In conclusion, therefore, we may say that for practical purposes we may disregard ether as an influential factor during the post-operative convalescence.

(f) *Digestive Leukocytosis.*—The diet is so restricted after major operations, for a time at least, that the digestive leukocytosis, which itself averages 33 per cent above normal, and is at its maximum three to four hours after the meal, need not be taken into consideration; on the other hand, the twenty-four to forty-eight hour starvation diet prescribed for patients upon whom laparotomies have been performed, must be given due weight, as it is well known that in fasting subjects there may be an increase of as much as 3,000 cells.

(g) *Primary or Intermediate Hemorrhage.*—An increase to 20,000 or 40,000 in the leukocytes, particularly the polymorphonuclear neutrophiles, is usually observed after severe hemorrhages, the degree of the leukocytosis depending very largely upon the quantity of blood lost, and its duration upon the rapidity with which the blood is regenerated. In the interpretation of a post-operative leukocytosis, one should bear in mind the effect of hemorrhage upon the white blood cell and inquire into the amount of blood lost during the operation. In but exceptional cases will this amount be large enough to have any appreciable effect upon the leukocytes; however, upon every hematologic chart, space should be reserved for the entry of a memorandum as to the loss of blood.

(h) *Imperfect Drainage.*—In the treatment of wounds already infected, or abscesses, drainage constitutes an important element. It happens occasionally that the drainage material is not adequate, or that a portion of the wound or abscess becomes walled off or separated from the general cavity so that its contents are not properly evacuated. This occurrence is very apt to be met with in abscesses in the peritoneal cavity, where, by the adhesion of one coat of intestine to another, a pocket is formed which is altogether, or in part, cut off from any communication with the main cavity. As will frequently happen, unless preventive measures are taken, the outlet of the wound or abscess becomes so small and contracted that the infected material becomes dammed up. No matter what the cause,whether it be improper material or faulty technique, insufficient drainage will make itself manifest by either a distinct rise in the white blood cells, or an interruption of the normal progressive fall. In a case in which an appendicial abscess was opened and drained, the record of the daily white blood count after the operation was as follows: 25,000, 29,000, 18,000, 19,000, 24,000 and 22,000. When after the third day the return of the leukocytes to normal was arrested, I suspected at once that the cavity was imperfectly drained, or that a pocket had become walled off, and when on the seventh day the leukocytosis had not fallen, I made an exploration under ether and discovered a collection of pus posterior to the bladder. The evacuation and drainage of this region was followed by a slow but progressive return to normal. There were in this case no symptoms which made me suspect a more serious complication, such as the rupture of the abscess into the peritoneal cavity, or the onset of a general peritonitis, and yet from the blood count it was evident that there were present conditions impeding the steps toward resolution. In this case, and I could cite many other illustrations, the blood count fluctuated for several days between 18,000 and 22,000, a phenomenon in itself ominous, and then jumped up to 40,000. On the last day the tension in the abscess was evidently so great that the purulent contents were being taken up by the circulation in such quantities as to give rise to this hyperleukocytosis.

(i) *Infection Within the Wound.*—In this connection we use the term infection in a more or less limited sense, and refer to the action of those pyogenic organisms only, which are responsible for the majority of infective wounds, viz: those of the streptococcic and staphylococcic group. Should any of these organisms gain access to the wound during the operation in sufficient quantities to give rise to an inflammatory process, the presence of such a process will in every case (exceptions but prove the rule) be revealed by the blood chart. Beginning not earlier than the third day there will be signs of the presence of conditions disturbing the normal course of the leukocytes. The normal course of the leukocytes has already been described, and is perfectly familiar to all those who have taken pains to observe the behavior of the leukocytes in the post-operative period. Whenever, therefore, the leukocytosis remains absolutely stationary or fluctuates, when it should return to normal, we have a positive indication for removing the dressing and examining the wound. The undesirability of frequent or meddlesome dressing of wounds is fully appreciated, so that any clinical sign, which directly points to the expediency of redressing the wound, should not be ignored.

(j) *Infection Without the Wound.*—In the post-operative period complications will arise which are due to secondary infection of tissues or organs distant from the wound itself. Thus, for example, in one of the tabulated cases an appendectomy (interval operation) was performed, and the wound healed throughout *per primam.* The daily blood count ran as follows: 30,000, 20,000, 17,000, 16,000, 15,000, 12,000, 16,000, 14,000, 13,000, 15,000 (pain in leg), 13,000 and 14,000 (elevation of temperature). When on the sixth day there was a rise of 4,000, and on the succeeding days a stationary or fluctuating leukocytosis, I was confident that a complication had arisen and that, though the life of the patient was not endangered, convalescence would be more or less protracted. Not till the fourth day after my suspicions were aroused did the patient begin to complain of pain in the left femoral region, when, upon examination, a phlebitis of the femoral and external iliac veins was discovered; not only did the rise in the leukocytosis precede the appearance of any subjective sign, but preceded as well the onset of fever. The temperature had returned to normal and the case was running an afebrile course when, on the fifth or sixth day there was a rise of two or three degrees. A careful continued record of the blood count is then of additional service, in that it warns us of an impending complication.

(k) *Affections of the General Peritoneal Cavity Complicating Operations or Injury of the Hollow Viscera.*—In the series of cases upon which these observations have been based, no opportunity was offered to observe the behavior of the white blood cells in the onset of a general septic peritonitis. Conclusions may, however, be drawn from the investigations that have been made in the study of the leukocytoses following intestinal perforation in typhoid fever. Given a case in which, either from the influence of traumatism or from imperfect apposition of the walls of the viscus, or indeed from infection, the contents escape into the general peritoneal cavity, conclusion as to the advisability or inadvisability of operation could be determined by frequently repeated (every one to three hours) observations of the blood. This should be instituted once the suspicion of the surgeon is aroused. Oftentimes before any pronounced subjective or objective manifestations of a general invasion of the peritoneal cavity have arisen, the blood count will indicate the spread of infection. Every surgeon is familiar with the dreadfully high mortality following operations for the relief of general peritonitis of many hours' duration, and in order that this mortality may be reduced, every measure should be called to our assistance which will warn us of the infection in its incipiency. Therefore after such operations as gastrostomy, gastro-enterostomy, cholecyst-enterostomy, cholecystotomy and the like, the surgeon should not fail to take advantage of such a valuable clinical sign as a rapidly rising leukocytosis.

Résumé.—In concluding my remarks upon the studies that have been made by Dr. Holloway and myself, I wish to express in emphatic terms the practical importance to the surgeon of the knowledge that may be derived from the observations of the blood count during the post-operative period. The criticism has too frequently been made that the blood count is unreliable and misleading, but if we should critically study the objections hitherto advanced against the employment of this clinical sign, we would find that in most instances too much has been expected. It is only right that we should regard the blood count as but a link in the chain of clinical evidence. It is quite as unjustifiable to assert that a diagnosis cannot be based upon the blood count as it is to assert that it cannot be based upon any other single clinical sign, subjective or objective. Those who have had much experience in the study of blood charts learn in time to properly interpret them and to place the proper valuation upon the individual records or series of records which have been taken of the case in question. I can readily understand how in inexperienced hands individual counts could have little or no meaning or be misinterpreted, and can understand how the significance of a complete series of blood counts could not be understood. One must be familiar with the conditions which give a rise or fall of the percentage of corpuscles or hemoglobin; one must recognize that there are certain physiologic as well as pathologic changes in the blood cells. I have called attention to the changes in the blood which have been noted by Dr. Holloway and myself during the post-operative period, and suggested in a very brief manner the application of these phenomena to practice. Little if any changes in the hemoglobin or in the erythrocytes were noted, although as careful records were kept of these as of the leukocytes. In uncomplicated cases the latter may be affected by drugs, ether, any condition causing concentration of the blood, by dressings and removal of drainage, by hemorrhage, by digestion. Complicated cases, imperfect drainage, infection within and without the wound and infection of the general peritoneal cavity are associated with a leukocytosis of greater or less degree. In the management of my cases in the postoperative period these records have been a source of great comfort, and I have felt that in them I had at my command evidence which lead me to suspect the presence of unfavorable conditions, and which often threw me on my guard before any other clinical evidence was at hand.

A Critical Review of the Figures Contained in the Appended Tables.

The blood examinations tabulated below were made from patients admitted to the general surgical wards of the University Hospital. No particular attention was given to the selection of these cases except that it was desired that in no case should there be a marked alteration of the normal blood picture.

As a consequence no case was taken that showed before operation any abnormality of the blood aside from a slight reduction or increase in the number of erythrocytes or the hemoglobin, or a hyperleukocytosis.

In a group of cases such as this, that represents to a fair degree the general run of ward cases, it is obviously a difficult matter to so classify them that the results may be of practical service and yet be accurately drawn from a hematological point of view.

Inasmuch as it is not the object of this paper to treat of the blood conditions associated with the various affections included in this series, but to deal with the effects of operation, it has been deemed advisable to classify them into Group A: Operative Cases, and Group B: Surgical procedures under ether without incision. While a number of other classifications have been made, they have been adopted only because of a desire to present accurate results.

Following the classification above given, out of the forty cases studied Group A would include from Case 1 to Case 33 inclusive and Group B from Case 34 to Case 40 inclusive.

In each instance the hemoglobin was estimated by the Fleischl hemoglobinometer, corpuscular counts made by the Thoma-Zeiss hemocytometer, while a sufficient number of spreads were made for subsequent staining and examination. In those instances where the count of erythrocytes or leukocytes seemed unusually high, second counts were made. For the differential counting five hundred cells were counted and in some few instances one thousand. In the study of the cells from two to four smears were examined.

The first count in each case was made within three hours of the time of operation except in those cases where a postponement of the operation prevented another count being made before the case was subjected to operative treatment.

The second count was made as soon after the effects of the ether had sufficiently passed away to permit of the necessary manipulations. Any restraint of the patient that could cause any congestion of the part from which the blood was to be taken was carefully avoided.

Subsequent counts were made each succeeding day until the leukocytes had returned to normal limits or until complications developed and rendered the ultimate return of the leukocytes too indefinite, or finally until the counts had to be necessarily discontinued.

Hemoglobin.—In a majority of the cases the hemoglobin showed a tendency to fluctuate and failed to make corresponding daily changes with the erythrocytes; in many instances this was slight. In 15 per cent of the cases where a fall occurred it was progressive, while in the remaining cases that showed a fall it was irregular.

The average hemoglobin percentage of the first estimations in these cases was 81.8, of the second 82.97, of the third 81.67, and of the last 79.33.

J. Chalmers DaCosta and Kalteyer (*Annals of Surgery*, September, 1901), in a series of fifty cases, found that the average hemoglobin percentage estimated in the majority of the cases within twenty-four hours before operation was eighty-nine, while eighty-six was the average percentage after ether, most of the estimations being made within twenty-four hours after the operation. In this series Oliver's hemoglobinometer was used.

The hemoglobin in our second estimation—first after operation—showed an increase over the first in 62.5 per cent of the cases with an average increase of 4 per cent; a decrease in 32.5 per cent with an average reduction of 4 per cent, while in 5 per cent of the cases it remained unchanged.

The third estimation gave an increase over the first in 42.5 per cent of the cases with an average rise of 3.4 per cent; a decrease in 47.5 per cent with an average fall of 3.1 per cent, while in 10 per cent of the cases no variation was noted.

In the last estimation 28.21 per cent of the cases demonstrated an increase, the average being 3.7 per cent; 58.97 per cent showed a decrease with 5.86 per cent as an average, while 12.82 per cent of the cases showed no change.

In Group A the average of the first estimations was 81.48 per cent, of the second 82.42 per cent, of the third 81.33 per cent, and of the last 78.87 per cent.

In Group B the averages for the first, second, third and last estimations were respectively 83.28, 85.57, 83.28 and 81.83 per cent.

Thirteen cases showed a progressive fall after first count.

Erythrocytes.—The erythrocytes before operation averaged 5,492,000, certainly a higher count than one would ordinarily expect to find.

In considering this one must look to the preparatory operative treatment, which, as is now well known, tends to cause a concentration of the blood. Probably the most important factors in this being the purgation and the withdrawal of food, as a consequence of which the output and income fail to maintain their normal relations.

The first and second counts after operation and the last count averaged respectively 5,584,000, 5,539,000 and 5,276,000.

In the second count 60 per cent of the cases showed an increase in the number of the erythrocytes over that recorded in the first. Of these 50 per cent gave an increase of 200,000 or more; 37.5 per cent an increase between 100,000 and 200,000, while in 12.5 per cent the rise was less than 100,000.

Of those cases in the second count—40 per cent—where the number of erythrocytes was reduced, 43.75 per cent showed a fall of 200,000 or more; 37.5 per cent gave a reduction between 100,000 and 200,000 and in 18.5 per cent the fall was less than 100,000.

Here as in the first count considerable stress must be placed upon the disturbed relations existing between the watery and cellular elements of the blood, the perspiration, vomiting and increased arterial pressure consequent upon the administration of the ether all tending to promote a blood concentration.

In the third count 47.5 per cent of the cases revealed an increase over the first erythrocytic count and 52.5 per cent a decrease.

Of those increased 42.11 per cent showed a gain of 200,000 or more; 21.05 per cent a rise of between 100,000 and 200,000, while in 36.84 per cent of the cases the gain was less than 100,000.

Of those decreased the fall was 200,000 or more in 47.62 per cent of the cases; between 100,000 and 200,000 in 33.33 per cent and less than 100,000 in 19.05 per cent.

The erythrocytic counts in the last examinations demonstrated an increase over those recorded in the first count in 33.33 per cent of the cases, while 66.67 per cent revealed a fall.

Of those increased, 61.54 per cent were increased 200,000 or more; 15.38 per cent showed a gain of between one and 200,000, while in 23.08 per cent there was an increase of less than 100,000.

In those cases showing a fall in the erythrocytes, 50 per cent gave a fall of 200,000 or more; 31.25 per cent, a fall between one and 200,000 and the number was reduced below 100,000 in 18.75 per cent of the cases.

In Group A the first counts gave an average of 5,477,000; the second 5,538,000; the third 5,516,000, while the last gave 5,215,000 erythrocytes per cubic millimetre.

As would be expected the greatest change between the average first and last counts occurred in this group, where the average loss in the last count was 262,000 cells.

If we were to divide this group into major and minor operations, the former including cases one to twenty-six inclusive and the latter cases twenty-seven to thirty-three inclusive, the major cases would show a loss of 288,000 between the average first and last counts, while the minor cases would give a diminution of 164,000 erythrocytes per cubic millimetre.

In Group B the average for the first count was 5,550,000, for the second 5,804,000, for the third 5,647,000, and for the last 5,610,000.

Here instead of the average last count giving a decreased number of cells there is an increase, but only one of 60,000.

In the stained specimens that were examined no marked or constant abnormal changes were noted subsequent to operation. In a few cases a slight irregularity in the size of the cells was observed, together with a moderate pallor; this was especially true in case number twenty.

In the last two examinations in this case a few polychromatophilic cells were seen.

In case number fifteen one normoblast was found in the last count, but its presence was unquestionably accidental and hardly deserves mention.

Considerable attention was given to determining the existence of basic degeneration as mentioned by Grawitz, but in no case could any cells be found that were affected by this interesting change. It should be mentioned however that thionin, which gave the best results for White and Pepper *Amer. Jour. Med. Sciences*, September, 1901), was not used as a stain in any of these cases.

Leukocytes.—In taking up the leukocytes in these cases we approach the factor that shows the greatest change and the one that is of most importance to the surgeon from a practical point of view.

For study the leukocytes will be divided into: (1) Leukocytes before operation; (2) Leukocytosis following operation.

Leukocytes before Operation.—Of all the cases enumerated below seven were malignant and gave an average leukocytosis of 14,022; twelve cases were inflammatory with an average of 12,498, while twenty-one were non-inflammatory in character and averaged 9,748.

In the malignant cases, except case number nineteen (leukocytes 32,160), the average would be but 11,000.

In this group all of the sarcomatous growths gave a leukocytosis, whereas in three of the four cases of a carcinomatous nature the leukocytes remained within normal limits; in the fourth case of carcinomatous character the leukocytes just exceeded the maximum normal limit accorded them.

Ewing, Cabot, Taylor and Sailer and others refer to the frequency of low counts in carcinomatous tumors of slow growth and superficial character, such as these cases were.

Those cases in Group A gave an average leukocytosis of 11,667; whereas 9,691 was the average of the leukocytes before operation in Group B.

Group A.—Of this group eleven cases involved the peritoneum—cases one to eleven inclusive—and gave an average leukocytosis of 11,294, the remaining twenty-two cases were non-peritoneal and involved various other structures; here 11,847 represents the average number of the white cells.

In the peritoneal cases four were inflammatory with an average leukocytosis of 15,055 and seven were non-inflammatory, the average being 9,165.

Three of the inflammatory cases were subacute, while case number six was acute and gave a leukocytosis of 21,180 cells per cubic millimetre.

Of the twenty-two non-peritoneal cases in Group A, four were inflammatory with an average white count of 12,240, seven were malignant with 14,022 leukocytes as an average, while eleven cases were of a non-inflammatory type, the average being 10,320 cells.

In Group B, in which by the subsequent operations no cutaneous incision was made, four cases were inflammatory—all chronic—and gave an average leukocyte count of 10,200, while three were non-inflammatory with an average of 9,013 cells per cubic millimetre.

Leukocytosis following Operation.—In considering the post-operative leukocytosis we must look to the effects of the ether as well as the operative procedure, since both of these contribute to the increase in the total number of cells per cubic millimetre. Just how much of this leukocytosis is due to one factor to the exclusion of the other it is impossible to determine.

Chadbourne (*Phil. Med. Jour.*, February, 1899), in a series of twenty-one cases found that after the administration of ether there was an increase in the number of leukocytes in each instance.

Cabot, Blake and Hubbard (*Annals of Surgery* September, 1901), found that in a series of fifty cases, there was an actual decrease in the number of leukocytes in seven cases, while in only thirteen cases was there an increase of more than 2,000 cells after full anesthesia. Unfortunately in this series the time of the leukocytic count before and after ether is not mentioned.

In the present series of forty cases, the first count after ether and operation in the malignant, non-inflammatory and inflammatory cases averaged respectively 24,777, 20,053 and 23,293 leukocytes per cubic millimetre.

If in the last of these we exclude case number five in which the leukocytes were exceedingly high —54,960—the series will average 20,414.

Those cases included in Group A, gave an average white count of 23,612, while in Group B the average number of leukocytes was 13,554. In the latter group case number thirty-eight gave a white count of 10,000, an increase of 2,000 over the first, while case number forty gave a leukocytosis of 17,280; an increase of 8,000 cells over those recorded in the count before ether.

Group A.—In regard to the peritoneal cases we found that the average white count was 28,385 leukocytes per cubic millimetre; except case number five above referred to, the average was 25,728.

The inflammatory peritoneal cases gave an average count of 35,200—excluding case five, an average of 28,613—while those of a non-inflammatory type had as their average 24,491 leukocytes.

The first post-operative count in the remaining twenty-two cases in this group resulted in an average of 21,225; the malignant cases averaging as above given, the four inflammatory 21,180, while the eleven cases of a non-inflammatory character gave an average count of 18,981 leukocytes.

Group B.—The four chronic inflammatory cases in this group gave an average leukocytic count of

13,500 cells, whereas the non-inflammatory cases averaged 13,626.

The averages taken in the same manner as the above all show a decrease in the second count after ether and operation over those recorded in the first post-operative count. In Group A, the greatest decrease being 11,000 in the inflammatory peritoneal cases while the smallest fall—2,000—occurred in the non-inflammatory cases in which the peritoneum was not involved in the operative treatment.

In Group B, both the inflammatory and non-inflammatory cases showed a fall of about 1,500 cells per cubic millimetre.

C. Y. White (UNIVERSITY MEDICAL MAGAZINE, June, 1900), in a series of twenty-eight celiotomy cases, gives 20,975 as his average for the first post-operative count and cites Taylor's average of 19,500 in twenty-two cases of celiotomies. In the cases here recorded the average of the peritoneal cases was 28,385. It should be mentioned in this comparison that in the counts taken by White the interval between the time of operation and the examination of the blood was about five hours longer than in the present series.

In all the cases in Group A that were not complicated by drainage, unfavorable conditions at the site of operation, or by other complications not involving the wound, the tendency was to a progressive fall in the leukocytes.

Bloodgood (*Medical News*, August, 1901), states that after the average operation the leukocytes return to normal within twenty-four hours. Cabot, Blake and Hubbard (*Annals of Surgery*, September, 1901), from complete counts in ten cases place the limit at thirty-six hours. White in his celiotomy series places his average at about five days.

In our series, in those uncomplicated operative cases where the count could be continued, three and a half days was the average time required for the leukocytes to return to 10,000 or less. In all the complicated operative cases the fall was more protracted, the leukocytes either remaining stationary for two or more days or fluctuating.

In cases with open wounds, where, at the time of dressing, drains were removed and the wound cleansed, there was frequently a rise in the leukocytes over the count of the preceding day, or it caused the count to remain stationary. In case three the development of a phlebitis caused an increase in the leukocytic count, while in case twenty-two the onset of an iodoform dermatitis was probably responsible for an increase in the number of leukocytes. In all the operative cases, except cases ten, twenty-six, twenty-eight, twenty-nine, thirty-two and thirty-three, the highest leukocytic count was recorded in the first examination after operation. In four of the above cases referred to it occurred in the second count — twenty-four hours — after operative treatment. In cases twenty-nine and thirty-two the second post-operative count was actually the highest, but the increase was so slight that it could hardly be considered.

By consulting the tabulated differential counts of the cases in Group A it will be observed that the greatest changes immediately following operation occurred in the polymorphonuclear cells and eosinophiles. The change affecting the former was consistent, for all the cases showed an absolute increase in the polymorphonuclear cells over those recorded in the first count. The eosinophiles were almost equally as consistent, but here instead of an increase there was an absolute decrease in 93.93 per cent of the cases, while in 57.57 per cent they were absent.

If this last percentage were based upon a constant five hundred cell count it would probably be somewhat higher, but in this series in several cases 1,000 cells were counted to observe the eosinophiles and where this was done they were found. In the subsequent count—except case ten where but three counts were made following operation—these cells returned and frequently in increasing numbers.

In Group B the cases also showed an increase in the number of polymorphonuclear neutrophiles, but the change in the eosinophiles was not as marked. In the first count after operation they were increased in two cases while in five the count demonstrated a diminution in their number. In but one instance were they absent and that occurred in case number forty which gave the highest leukocytic count in this group.

In reference to the size and staining qualities of the various cells, it may be briefly stated that all were within normal requirements; the same holds true in reference to granulations in those cases possessing granular protoplasm.

A number of apparently vacuolated polymorphonuclear, mononuclear and transitional cells were observed. Usually this was observed in the protoplasm, but in a few instances the nucleus of the mononuclear or transitional cell was involved.

A large number of broken cells and leukocytic shadows were also observed.

A TABULATED REPORT OF THE BLOOD ANALYSIS OF FORTY CASES.

CASE 1.—MR. E., APPENDICITIS (APPENDECTOMY).

Date.	No. Counts.	Temperature.	Hemoglobin.	Erythrocytes.	Leukocytes.	Polymorpho-nuclear.	Lymphocytes.	Mononuclear.	Transitional.	Eosinophiles.	Remarks.
3-7	*a*	98	90	5,260,000	8,880	76.2% 6,767	17% 1,510	1.4% 124	4.6% 408	.8% 71	Urine: Amber; cloudy; acid; 1,026; no albumin or sugar; amorphous urates.
3-7	*b*	98.4	90	5,310,000	16,320	84.2% 13,742	10.4% 1,697	.6% 98	3.8% 620	1% 163	First count after operation. No vomiting.
3-8	*c*	99.2	88	5,730,000	13,200	85.6% 11,299	8.8% 1,162	1.6% 211	3.8% 502	.2% 26	Fluids taken, fl. oz. v; urine voided, fl. oz. xxxv.
3-9	*d*	99.4	92	5,520,000	15,360	77.4% 11,889	14.6% 2,242	1.4% 215	5.8% 891	.8% 123	Fluids taken, fl. oz. viii; urine voided, fl. oz. xxxii; stools, i; comfortable since operation; considerable distension to-day; peristalsis good.
3-10	*e*	99.2	86	5,290,000	9,840	71.2% 7,006	19.8% 1,948	1% 99	6.4% 630	1.6% 157	Fluids taken, fl. oz. xviii; urine voided, fl. oz. xxiii; stools, i.
3-11	*f*	98.4	86	5,540,000	9,600	68.6% 6,585	20.8% 1,997	1.8% 173	6.8% 653	2% 192	Fluids taken, fl. oz. xlviii; urine voided, fl. oz. xx; patient comfortable.

CASE 2.—MR. P., RECURRENT APPENDICITIS (APPENDECTOMY).

11-15	*a*	98.2	80	5,740,000	9,440	62.5% 5,900	26.1% 2,464	1.9% 179	5.2% 491	4.3% 406	Urine: Amber; clear; acid; 1,020; no albumin or sugar.
11-15	*b*	98.8	83	5,860,000	18,640	91.2% 17,000	4.73% 881	1.27% 237	2.73% 509	.07% 13	First count after operation; vomited fl. oz. iv.
11-16	*c*	99.4	77	5,440,000	16,400	85.8% 14,071	9.2% 1,509	8% 131	3.6% 591	.6% 98	No sleep during night; some pain; fluids taken, fl. oz. xxix; urine voided, fl. oz. xxvii.
11-17	*d*	99.2	76	5,150,000	13,520	79% 10,681	12.5% 1,690	1.34% 181	5.33% 721	1.83% 247	Patient comfortable; stools, i.
11-18	*e*	98.6	78	4,670,000	9,520	76.6% 7,292	13.2% 1,257	1.8% 171	4.6% 438	3.8% 362	Comfortable; has not been dressed; stools, ii.

CASE 3.—MR. Z., APPENDICITIS (APPENDECTOMY).

7-7	*a*	98.8	89	5,420,000	13,120	76.6% 10,050	15.2% 1,994	1.4% 184	6.4% 840	.4% 52	Urine: Amber; clear; 1,023; no albumin or sugar.
7-7	*b*	98.4	86	5,620,000	30,720	90% 27,648	3% 921	.8% 246	6.2% 1,905	....	First count after operation.
7-8	*c*	99.8	90	5,810,000	20,320	82.2% 16,703	7.4% 1,504	2.2% 447	8.2% 1,666	....	Some distention; very slight pain at seat of wound; fluids taken, fl. oz. v; urine voided, fl. oz. xii; stools, i.
7-9	*d*	98.6	86	5,760,000	17,200	74% 12,728	15% 2,580	.6% 103	9% 1,548	1.4% 241	Fluids taken, fl. oz. xx; urine voided, fl. oz. xix; stools, ii; abdomen flat; peristalsis good.
7-10	*e*	98	87	5,570,000	16,000	65.7% 10,512	21% 3,360	2.5% 400	9.6% 1,536	1.2% 192	Fluids taken, fl. oz. xxi; urine voided, fl. oz. xxii.
7-11	*f*	98.6	82	5,590,000	15,040	75.7% 11,385	18.3% 2,752	1.3% 196	4% 602	.7% 105	Fluids taken, fl. oz. xxxviii; urine voided, fl. oz. xxx; comfortable.
7-12	*g*	98.4	81	5,730,000	15,280	72.6% 11,093	14.8% 2,262	2.4% 367	8.6% 1,314	1.6% 244	Not dressed; very comfortable; sleeps well; some itching at site of incision.
7-13	*h*	......	86	5,870,000	12,160	68.2% 8,293	21.8% 2,651	1% 122	6.4% 778	2.6% 316	
7-14	*i*	......	83	5,720,000	16,560	75.7% 12,536	18.3% 3,030	1.3% 215	4% 663	.7% 116	Dressed to-day for first time; no pus; all stitches removed.
7-15	*j*	......	89	5.660,000	14,040	75% 10,530	13% 1,825	1.2% 168	8.6% 1,208	2.2% 309	
7-16	*k*	......	87	5,860,000	13,760	73.25% 10,079	12.75% 1,755	1.5% 206	11.75% 1617	.75% 103	
7-18	*l*	......	84	5,770,000	15,840	73.75% 11,682	19.25% 3,049	.75% 119	4.50% 713	1.75% 277	Slight pain in leg.
7-20	*m*	99.8	85	5,740,000	13,040	72.6% 9,467	17.4% 2,269	1.6% 209	5.6% 730	2.8% 365	Pain in leg persists, and more marked.
8-4	*n*	98.4	82	5,780,000	14,480	73.4% 10,628	16.6% 2,404	1.6% 232	6.2% 898	2.2% 318	Phlebitis discovered 7-21.

CASE 4.—MR. McC., APPENDICITIS (APPENDECTOMY).

(Tip of appendix distended by accumulation of pus; ruptured during manipulation.

Date.	No. Counts.	Temperature.	Hemoglobin.	Erythrocytes.	Leukocytes.	Polymorpho-nuclear.	Lymphocytes.	Mononuclear.	Transitional.	Eosinophiles.	Remarks.
3–7	*a*	97	94	5,770,000	12,880	78.2% 10,072	13.6% 1,752	1.0% 129	7% 901	.2% 26	Urine, amber; whitish precipitate; alkaline. 1,025; no albumin or sugar; phosphates.
3–7	*b*	97.2	89	5,720,000	29,200	86.4% 25,299	6.4% 1,869	1% 292	6.2% 1,810	....	First count after operation; no vomiting; gauze drainage.
3–8	*c*	98.6	93	5,720,000	22,560	82.2% 18,544	9.4% 2,121	1.2% 271	7% 1,579	.2% 45	Fluids taken, fl. oz. v; urine voided, fl. oz. xxxiv.
3–9	*d*	98.6	91	5,410,000	16,960	79.4% 13,466	11.8% 2,001	.8% 136	7.5 1,272	.5% 85	Fluids taken, fl. oz. xxv; urine voided, fl. oz. xx; stools, i; slight abdominal pain; no distention; peristalsis good.
3–10	*e*	98.6	89	5,780,000	12,480	76.2% 9,510	14.2% 1,772	1.4% 175	7.4% 923	.8% 100	Fluids taken, fl. oz. xxi; urine voided, fl. oz. x+; patient comfortable.
3–11	*f*	99	92	5,460,000	15,360	75.4% 11,581	13.8% 2,120	2.4% 369	7% 1,075	1.4% 215	Fluids taken, fl. oz. liv; urine voided, fl. oz xvii; dressed to-day and gauze drainage removed; no pus.
3–12	*g*	99	90	5,620,000	11,120	68.8% 7,650	20.8% 2,313	2% 222	4.6% 512	3.8% 423	Fluids taken, fl. oz. xliii; urine voided, fl. oz. xviii; stools, i; patient comfortable.
3–13	*h*	98	90	5,310,000	12,080	71.2% 8,601	17.6% 2,126	1.2% 145	8.8% 1,063	1.2% 145	Fluids taken, fl. oz. liv; urine voided, fl. oz. xxxii; stools, i.

CASE 5.—MR. P., APPENDICITIS (APPENDECTOMY).

(Accumulation of pus, size of pea, in appendix; not ruptured.

Date.	No. Counts.	Temperature.	Hemoglobin.	Erythrocytes.	Leukocytes.	Polymorpho-nuclear.	Lymphocytes.	Mononuclear.	Transitional.	Eosinophiles.	Remarks.
12–7	*a*	98.8	85	5,780,000	13,040	78.2% 10,197	16.8% 2,191	.2% 26	4.6% 600	.2% 26	Urine: Amber; cloudy; alkaline; 1030; no albumin or sugar.
12–7	*b*	97.8	83	5,590,000	54,960	90.4% 49,684	4% 2,198	1% 550	4.6% 2,528	....	First count after operation; vomited fl. oz. iii.
12–8	*c*	99.8	85	6,040,000	22,800	85.4% 19,471	7.6% 1,733	1.2% 274	5.4% 1,231	.4% 91	Fluids taken, fl. oz. xxxvi; urine voided, fl. oz. viii; catheterized; few peristaltic sounds heard.
12–9	*d*	99	80	6,090,000	19,360	78.4% 15,178	13.6% 2,633	2% 387	5.8% 1,123	.2% 39	Patient quite comfortable.
12–10	*e*	99	80	5,760,000	13,520	59.6% 8,058	25.2% 3,407	2.4% 325	12% 1,622	.8% 108	Dressed to-day; wound healing by first intention.
12–11	*f*	98.4	79	5,310,000	12,320	66% 8,131	19.6% 2,415	3.2% 394	9.8% 1,207	1.4% 173	

CASE 6.—MR. H., APPENDICEAL ABSCESS (APPENDECTOMY).

Date.	No. Counts.	Temperature.	Hemoglobin.	Erythrocytes.	Leukocytes.	Polymorpho-nuclear.	Lymphocytes.	Mononuclear.	Transitional.	Eosinophiles.	Remarks.
5–14	*a*	99	90	4,840,000	21,180						
5–14	*b*	97.2	85	5,270,000	25,920	86.6% 22,447	5% 1,296	.6% 155	7.8% 2,022	....	First count after operation; gauze drainage.
5–15	*c*	99.8	86	4,970,000	29,760	88% 26,189	4.6% 1,369	1.20% 357	5.6% 1,667	.6% 178	Fluids taken, fl. oz. iv; urine voided, fl. oz. xviii; patient quite restless.
5–16	*d*	99	82	5,100,000	18,320	78.2% 14,326	9% 1,649	2.4% 440	10.2% 1,869	.2% 36	Fluids taken, fl. oz. xx; urine voided, fl. oz. xxiv; stools, i; wound dressed to-day; edges slightly red.
5–17	*e*	98.8	82	5,290,000	19,120	84.4% 16,137	8.8% 1,683	.6% 115	5.2% 994	1% 192	Fluids taken, fl. oz. xxiv; uzine voided, fl. oz. xxi; dressed and one piece of gauze removed.
5–18	*f*	98.8	79	4,820,000	24,400	80.8% 19,715	9.4% 2,294	1% 244	8% 1,952	.8% 195	Dressed and new drainage inserted; abdominal pain.
5–19	*g*	99.4	78	4,620,000	22,320	76.6% 17,097	12.4% 2,768	1% 223	9% 2,009	1% 223	Abdominal pain; abdomen distended; dressed.
5–20	*h*	97.4	79	4,600,000	40,880	87.2% 35,647	6% 2,453	.8% 327	6% 2,453	....	After secondary operation; large pocket of pus found and evacuated.

CASE 7.—Mr. C., Incomplete Oblique Inguinal Hernia (Bassini's Operation).

Date.	No. Counts.	Temperature.	Hemoglobin.	Erythrocytes.	Leukocytes.	Polymorpho-nuclear.	Lymphocytes.	Mononuclear.	Transitional.	Eosinophiles.	Remarks.
2-15	*a*	98.1	85	5,570,000	8,080	74% 5,979	18.4% 1,487	1.4% 113	4% 323	2.2% 178	Urine: Amber; clear; acid; 1035; no albumin or sugar.
2-15	*b*	98	86	5,900,000	27,840	89% 24,778	7.2% 2,004	1% 278	2.8% 780	....	Fluids taken, fl. oz. iv; urine voided, fl. oz. vi.
2-16	*c*	100	83	5,640,000	18,640	77.8% 14,502	11.6% 2,162	2.4% 448	8% 1,491	.2% 37	Fluids taken, fl. oz. xvi; urine voided, fl. oz. xiv.
2-17	*d*	99	88	5,910,000	15,120	77.8% 11,763	12.2% 1,845	1.6% 242	8.4% 1,270	....	
2-18	*e*	98.1	84	5,420,000	14,880	76.6% 11,398	13.4% 1,994	1.4% 208	8.2% 1,220	.4% 60	No unfavorable symptoms.
2-19	*f*	98	87	5,300,000	8,800	69.4% 6,107	19.2% 1,690	1% 88	8% 704	2.4% 211	Fluids taken, fl. oz. xxxii; urine voided, fl. oz. xxviii; stools, i.

CASE 8.—Mr. J., Incomplete Inguinal Hernia (Bassini's Operation).

2-15	*a*	98	88	5,680,000	9,200	73.4% 6,753	18.8% 1,730	1.8% 165	5% 460	1% 92	Fluids taken, fl. oz. iii; urine voided, fl. oz. xxii; stools, ii; Urine: Acid; clear; amber; 1025; no albumin or sugar.
2-15	*b*	97.2	82	5,850,000	24,080	90.6% 21,816	5.8% 1,397	.2% 48	3.4% 819	....	First count after operation.
2-16	*c*	99.8	85	5,820,000	18,160	85% 15,436	9.2% 1,671	1.2% 218	4.4% 799	.2% 36	Fluids taken fl. oz. xxxii; urine voided, fl. oz. xii.
2-17	*d*	98.4	81	5,940,000	14,080	71.2% 10,025	18.4% 2,591	1% 141	7.6% 1,070	1.8% 253	Fluids taken, fl. oz. xxxvi; urine voided, fl. oz. xviii.
2-18	*e*	98.8	79	5,660,000	12,320	65.8% 8,107	23.8% 2,932	1.2% 148	7.8% 961	1.4% 172	Fluids taken, fl. oz. xxxvi; urine voided, fl. oz xxiii; stools, i.
2-19	*f*	98.6	85	5,510,000	9,600	73.8% 7,085	16% 1,536	2.2% 211	7% 672	1% 96	Fluids taken, fl. oz. l; urine voided, fl. oz. xviii.
2-20	*g*	98.6	82	5,550,000	8,240	70.0% 5,768	19.2% 1,582	1.2% 99	8.4% 692	1.2% 99	

CASE 9.—Mr. S., Complete Inguinal Hernia (Bassini's Operation).

3-6	*a*	99	86	5,650,000	9,680	63.8% 6,176	26.8% 2,594	1.2% 116	7% 678	1.2% 116	Urine: Amber; clear; neutral; 1030; no albumin or sugar; phosphates.
3-6	*b*	98	92	5,970,000	31,280	87.4% 27,339	9.6% 3,003	.6% 187	2.4% 751	....	First count after operation.
3-7	*c*	99.4	90	5,430,000	20,160	82.6% 16,652	10.6% 2,137	.6% 121	6% 1,210	.2% 40	Fluids taken, fl. oz. xxx; urine voided, fl. oz. x; no pain or distention; patient quite comfortable.
3-8	*d*	99	90	5,750,000	22,000	80.6% 17,732	11% 2,420	1.8% 396	6.2% 1,364	.4% 88	Fluids taken, fl. oz. xxvi; urine voided, fl. oz. xxv; stools, ii.
3-9	*e*	98.6	84	5,860,000	14,480	71.4% 10,339	21% 3,041	1.2% 174	5.4% 782	1% 144	Fluids taken, fl. oz. xxxvi; urine voided, fl. oz. xxv.
3-10	*f*	98.4	89	3,810,000	12,560	67.8% 8,516	24.4% 3,065	1.6% 201	5.2% 653	1% 125	Fluids taken, fl. oz. xlviii; urine voided, fl. oz. xxix; stools, ii.
3-11	*g*	98.4	86	5,540,000	11,200	67.8% 7,594	21.6% 2,419	1.4% 157	7% 784	2.2% 246	Fluids taken, fl. oz. xlii; urine voided, xii+.
3-12	*h*	98.6	85	5,840,000	9,600	65.4% 6,279	23.4% 2,246	.6% 58	7.4% 710	3.2% 307	

CASE 10.—Mr. R., Left Inguinal Hernia (Bassini's Operation).

11-27	*a*	98.6	72	4,880,000	9,600	57.2% 5,491	30.8% 2,957	2.2% 211	8.6% 826	1.2% 115	Urine: Amber; clear; acid; 1012; no albumin or sugar.
11-29	*b*	97.6	70	5,110,000	9,760	56.2% 5,485	32.8% 3,201	2.8% 273	6% 586	2.2% 215	
11-29	*c*	98	82	5,180,000	21,440	87.8% 18,824	6.8% 1,458	.6% 129	4.8% 1,029	....	First count after operation.
11-30	*d*	100.8	74	5,630,000	26,880	89.8% 24,138	7% 1,882	.6% 161	2.6% 699	....	Fluids taken, fl. oz. xx; urine voided, fl. oz. xix; complained of pain in left testicle and wound; tore off dressing.
12-1	*e*	102.8	80	5,325,000	21,360	89.4% 19,096	6.2% 1,324	1.2% 256	3.2% 684	....	Fluids taken, fl. oz. lxi; urine vioded, fl. oz xv+; dressed; tenderness and swelling of left testicle; pus found 12-3-01.

CASE 11.—Mr. F., Double Inguinal Hernia (Bassini's Operation on Right Side).

Date.	No. Counts.	Temperature.	Hemoglobin.	Erythrocytes.	Leukocytes.	Polymorphonuclear.	Lymphocytes.	Mononuclear.	Transitional.	Eosinophiles.	Remarks.
2–21	*a*	98.8	81	5,690,000	9,120	81.6% 7,442	11% 1,003	.6% 55	4.4% 401	2.4% 219	Urine: Amber; acid; 1025; no albumin or sugar.
2–21	*b*	97.8	76	5,850,000	31,840	92.6% 29,484	3.2% 1,019	.4% 127	3.8% 1,210	....	First count after operation.
2–22	*c*	102.2	79	5,750,000	17,200	92.8% 15,962	3% 516	.2% 34	4% 688	....	Considerable pain, and some vomiting after milk taken; peristalsis good.
2–23	*d*	101.2	83	5,550,000	22,960	92.2% 21,169	3.2% 735	1.6% 367	3% 689	....	Wound opened and considerable sanguineous fluid evacuated; upper angle of wound involved; edges flushed; considerable tenderness; extending upward from wound (upper angle) tissues were laid open for three inches
2–24	*e*	99.8	78	5,490,000	21,120	93.6% 19,768	2.2% 465	.4% 84	3.8% 803	....	Since yesterday wound has been dressed frequently; flush marked.
2–26	*f*	99	76	5,540,000	17,040	90.2% 15,370	4% 682	.8% 136	4.6% 784	.4% 68	Patient very drowsy; at times delirious; tongue brown and dry; flush and induration not so marked. Urine: Amber; flocculent precipitate; acid; 1025; albumen ⅛ by bulk; no sugar.
2–28	*g*	100	77	5,400,000	43,760	93.2% 40,784	3% 1,313	.6% 263	3% 1,313	.2% 87	Slight vomiting; hiccough.

CASE 12.—Mr. B., Tic Douloureux (Avulsion of Gasserian Ganglion).

Date.	No. Counts.	Temperature.	Hemoglobin.	Erythrocytes.	Leukocytes.	Polymorphonuclear.	Lymphocytes.	Mononuclear.	Transitional.	Eosinophiles.	Remarks.
4–25	*a*	98.2	80	4,880,000	9,120	64.6% 5,891	23% 2,098	1.6% 146	9.2% 839	1.6% 146	
4–25	*b*	97	72	4,820,000	26,880	85.8% 23,063	7% 1,881	.2% 54	6.8% 1,828	.2% 54	First count after operation; gauze drainage.
4–26	*c*	99.8	69	4,190,000	20,800	83.2% 17,306	11% 2,288	.2% 41	5.6% 1,165	....	Fluids taken, fl. oz. xx; urine voided, fl. oz. xx.
4–27	*d*	98.6	70	4,520,000	15,680	73% 11,446	16% 2,509	.8% 125	8.8% 1,380	1.4% 220	Fluids taken, xxiv; urine voided, xxiv; stools, ii; patient quiet and free from pain; dressed, but packing not removed.
4–28	*e*	99.2	65	4,120,000	14,000	72% 10,080	18.4% 2,576	1% 140	7.8% 1,092	.8% 112	Fluids taken, fl. oz. xxiv; urine voided, fl. oz. xxiii; no pain; packing loosened.
4–29	*f*	98.8	65	4,780,000	14,000	66.2% 9,268	19.4% 2,716	1.4% 196	11.2% 1,568	1.8% 252	Fluids taken, fl. oz. xxiv; urine voided, fl. oz. xvii; one piece of packing removed.
4–30	*g*	98.8	62	4,280,000	14,480	71.8% 10,397	17.2% 2,490	.4% 58	9% 1,303	1.6% 232	Fluids taken, fl. oz. xxx; urine voided, fl. oz xiv; stools, i.
5–1	*h*	99.2	64	4,460,000	14,400	75.6% 10,886	13.4% 1,930	.6% 86	8.4% 1,210	2% 288	Wound presents brawny appearance; fluids taken, fl. oz. xxxvi; urine voided, fl. oz. xxvi.
5–2	*i*	98.6	63	4,080,000	11,360	62% 7,043	23.4% 2,658	1.8% 205	10.8% 1,227	2% 227	Gauze still being used in wound; fluids taken, fl. oz. xl; urine voided, fl. oz. xxix.

CASE 13.—Mr. K., Epilepsy (Trephining).

Date.	No. Counts.	Temperature.	Hemoglobin.	Erythrocytes.	Leukocytes.	Polymorphonuclear.	Lymphocytes.	Mononuclear.	Transitional.	Eosinophiles.	Remarks.
6–1	*a*	98	80	5,870,000	10,000	65% 6,500	29.4% 2,940	1% 100	4% 400	.6% 60	Urine: Clear; amber; acid; 1022; mucus; leukocytes; no albumin or sugar.
6–1	*b*	97.2	78	5,450,000	14,320	68.2% 9,766	25.8% 3,695	.4% 57	5.6% 802	....	First count after operation; vomited fl. oz. vi
6–2	*c*	99.2	76	5,400,000	10,800	71.2% 7,690	21.4% 2,311	1% 108	5.2% 561	1.2% 130	Quite comfortable.
6–3	*d*	98.8	78	5,400,000	9,360	60.6% 5,672	27.6% 2,583	1.8% 169	7.8% 730	2.2% 206	No unfavorable symptoms.
6–4	*e*	98.2	81	5,280,000	8,800	63.8% 5,615	28.2% 2,482	.8% 70	6.4% 563	.8% 70	Out of bed; no pain since operation.

CASE 14.—Mr. W., Epilepsy (Trephining).

Date.	No. Counts.	Temperature.	Hemoglobin.	Erythrocytes.	Leukocytes.	Polymorpho-nuclear.	Lymphocytes.	Mononuclear.	Transitional.	Eosinophiles.	Remarks.
12-5	*a*	97.8	72	5,450,000	14,640	70.6% 10,336	23.4% 3,426	.4% 59	4.6% 673	1% 146	Urine: Amber; clear; acid; 1024; no albumin or sugar.
12-7	*b*	97.4	75	5,660,000	15,760	67.8% 10,685	23.8% 3,751	.6% 94	6.4% 1,009	1.4% 221	
12-7	*c*	96.4	84	5,540,000	28,240	87.2% 24,625	5.8% 1,638	.6% 170	6.2% 1,751	.2% 56	First count after operation; vomited fl. oz. ii mucus and blood; gauze drainage.
12-8	*d*	98.6	80	5,560,000	14,960	76.2% 11,399	15.8% 2,364	1.6% 239	5.4% 808	1% 150	Fluids taken, fl. oz. xli; urine voided, fl. oz. x.
12-9	*e*	98.4	76	5,450,000	13,280	71% 9,429	19% 2,523	1.38% 183	8.12% 1,078	.5% 67	Fluids taken, fl. oz. xxiii; urine voided, fl. oz. xvi; stools, ii; light diet.
12-10	*f*	98.4	75	5,000,000	14,400	72.4% 10,425	20.6% 2,966	1.4% 202	4.4% 634	1.2% 173	Fluids taken, fl. oz. xviii; urine voided, fl. oz. xxxvi; stools, i; dressed to-day, and gauze drainage removed.
12-11	*g*	98.8	79	4,930,000	13,280	75.6% 10,040	16.8% 2,231	1.2% 159	6.2% 823	.2% 27	Wound clean.

CASE 15.—Mr. P., Traumatic Epilepsy (Trephining).

4-19	*a*	98.4	78	5,930,000	9,440	69.4% 6,551	21.8% 2,058	1% 95	6.2% 585	1.6% 151	Urine: Amber; cloudy; alkaline; 1030; no albumin or sugar; phosphates; mucous; few leukocytes.
4-19	*b*	99.2	79	5,830,000	12,880	88.8% 11,437	7.8% 1,005	.4% 52	3% 386	....	First count after operation.
4-20	*c*	98.6	85	5,570,000	12,800	73.8% 9,446	15.2% 1,946	.8% 102	7.2% 722	3% 384	Fluids taken, fl. oz. xxxvi; urine voided, fl. oz. xxviii.
4-21	*d*	99	81	5,820,000	9,920	69.6% 6,905	21% 2,083	1% 99	5.8% 575	2.6% 258	Fluids taken, fl. oz. xlviii; urine voided, fl. oz. xxiv; stools, i.
4-22	*e*	98.4	80	5,380,000	9,120	63% 5,746	27.5% 2,508	1.5% 137	4.75% 433	3.25% 296	Light diet.

CASE 16.—Mr. M., Epilepsy (Trephining).

4-17	*a*	98.4	81	5,980,000	9,200	68.4% 6,293	24% 2,208	.6% 55	7% 644	....	Urine: Amber; cloudy; alkaline; 1030; no albumin or sugar.
4-17	*b*	97.4	82	5,930,000	15,760	89.4% 14,090	5.8% 914	.4% 63	4.4% 693	....	First count after operation; gauze drainage.
4-18	*c*	99.2	84	5,960,000	12,240	77.4% 9,474	15.2% 1,860	1.8% 220	5.6% a 686	....	Fluids taken, fl. oz. xxiv; urine voided, fl. oz. xv.
4-19	*d*	98.4	82	5,940,000	12,080	78.6% 9,495	11.6% 1,401	.8% 97	8.4% 1,015	.6% 72	Fluids taken, fl. oz. xxxii; urine voided, fl. oz. xxxiii; stools, i.
4-20	*e*	98.6	80	5,630,000	8,640	74.5% 6,437	19% 1,642	2% 173	3.5% 302	1% 86	
4-21	*f*	98	79	5,360,000	8,960	65.4% 5,860	28.8% 2,580	.8% 72	4.6% 412	.4% 36	

CASE 17.—Mr. B., Recurrent Epithelioma (Excision of Secondary Growth in Neck).

2-8	*a*	98.4	72	5,020,000	11,360	71% 8,066	18.8% 2,136	1% 113	5.6% 636	3.6% 409	Urine: Amber; clear; acid; 1033; no albumin or sugar.
2-8	*b*	97	74	4,750,000	27,040	91.4% 24,715	3% 811	.8% 216	3.8% 1,028	1% 270	First count after operation; drainage in lower portion of wound.
2-9	*c*	99	75	4,700,000	13,840	76.8% 10,629	13.4% 1,855	2.2% 305	6% 830	1.6% 221	Fluids taken, fl. oz. xxxiv; urine voided, fl. oz. xxii.
2-10	*d*	98	74	4,910,000	17,200	69.2% 11,902	16.2% 2,787	2.4% 413	7.6% 1,307	4.6% 791	Fluids taken, fl. oz. xlv; urine voided, fl. oz. xxxvi; stools, ii; dressed to-day and drainage removed; wound clean.
2-11	*e*	98.8	74	4,990,000	9,360	74.4% 6,964	14.8% 1,385	.6% 56	4.6% 431	5.6% 524	Patient comfortable.
2-12	*f*	98.4	73	4,910,000	8,605	64.8% 5,547	20% 1,712	1.2% 103	8.2% 702	5.8% 496	Light diet.
2-13	*g*	97.8	71	4,760,000	7,760	64% 4,967	24.5% 1,901	1.7% 132	5.3% 411	4.5% 349	

CASE 18.—Mrs. G., Scirrhous Carcinoma of Breast (Breast Portion of Pectoralis Major Muscle and Axillary Glands Removed).

Date.	No. Counts.	Temperature.	Hemoglobin.	Erythrocytes.	Leukocytes.	Polymorphonuclear.	Lymphocytes.	Mononuclear.	Transitional.	Eosinophiles.	Remarks.
1-16	*a*	99	78	4,040,000	9,920	66.4% 6,587	23.4% 2,321	1.6% 159	8% 794	.6% 59	First count after operation.
1-17	*b*	97	76	4,320,000	20,640	90.3% 18,638	4.45% 918	.9% 186	4.35% 898	....	Fairly comfortable to-day; no pain at site of wound.
1-18	*c*	100.4	82	5,020,000	12,400	76% 9,424	15% 1,860	1.8% 223	7% 868	.2% 25	Dressed to-day, and upon separating edges of wound, about fl. oz. ½ of blood escaped from wound.
1-19	*d*	100.2	75	4,350,000	10,000	75.2% 7,520	15.6% 1,560	2.2% 220	6.2% 620	.8% 80	Comfortable.
1-20	*e*	99.6	73	4,490,000	9,600	70.2% 6,739	20.6% 1,978	.8% 77	7% 672	1.4% 134	Comfortable; no pain; wound clean.
1-21	*f*	99.6	72	4,020,000	8,880	72.4% 6,429	17.8% 1,581	1.6% 142	6.8% 604	1.4% 124	

CASE 19.—Mr. D., Lympho-Sarcoma involving Mediastinum and Left Side of Neck (Removal of Supraclavicular Mass).

Date.	No. Counts.	Temperature.	Hemoglobin.	Erythrocytes.	Leukocytes.	Polymorphonuclear.	Lymphocytes.	Mononuclear.	Transitional.	Eosinophiles.	Remarks.
12-14	*a*	99	74	5,940,000	26,240	79.4% 26,240	12.6% 3,306	1.1% 288	6.4% 1,679	.5% 131	Left hand.
12-16	*b*	99.2	77	6,265,000	31,680	87.9% 27,846	6.6% 2,090	.7% 221	4.7% 1,488	.1% 31	Right hand; gland removed under local anasthesia.
12-17	*c*	98.4	78	6,365,000	35,520	84.5% 30,014	6.1% 21,66	.9% 319	8.1% 2,877	.4% 142	Right hand.
12-18	*d*	98.8	73	6,110,000	27,600	81.2% 22,411	10.2% 2,815	1% 276	7.2% 1,987	.4% 111	Right hand; wound dressed.
1-2	*e*	99.4	74	5,980,000	25,120	76.9% 19,317	12.1% 3,039	1.5% 376	8.% 2,009	1.5% 376	Right hand.
1-3	*f*	99	76	6,090,000	32,160	83.4% 32,160	9.3% 2,926	.6% 192	6.6% 2,122	.3% 96	Right hand; before operation.
1-3	*g*	97.4	77	5,860,000	47,840	92.5% 44,252	2.95% 1,411	.25% 119	4.3% 2,057	....	First count after operation; right hand; no vomiting after ether; drainage in wound.
1-4	*h*	102.6	72	5,980,000	43,760	89% 38,946	4.8% 2,100	.8% 350	5.4% 2,363	....	Right hand; free perspiration.
1-5	*i*	102.4	76	5,840,000	37,760	81% 30,585	8.1% 3,058	1.5% 566	9.4% 3,549	....	Right hand; dressed and one stitch removed; free perspiration; edges of wound flushed; tube filled with turbid fluid.
1-6	*j*	102	77	5,740,000	34,720	81.9% 28,435	5.5% 1,909	1.3% 451	10.8% 3,749	.5% 173	Right hand; dressed; face flushed and perspiration marked.
1-7	*k*	104	76	5,810,000	28,960	87.973% 24,476	3.062% 886	1.285% 370	7.616% 2,203	.062% 1%	Right hand; face markedly flushed and perspiration free; dressed; discharge not marked; considerable redness about wound.
1-21	*l*	103.6	70	4,660,000	31,760	84.6% 26,869	10.2% 3,240	.4% 127	4% 1,270	.8% 254	Right hand; free perspiration continues; tongue coated; pulse dicrotic; dressed.
2-2	*m*	101.4	....	....	46,880	87.8% 41,160	6.2% 2,906	1% 468	5% 2,344	....	Right hand.

CASE 20.—Mr. H., Osteo-Sarcoma Humerus (Complete Amputation Upper Extremity).

Date.	No. Counts.	Temperature.	Hemoglobin.	Erythrocytes.	Leukocytes.	Polymorphonuclear.	Lymphocytes.	Mononuclear.	Transitional.	Eosinophiles.	Remarks.
2-7	*a*	98.6	72	5,390,000	13,200	68.6% 9,055	20.8% 2,746	4% 53	10% 1,320	.2% 26	Urine: no albumin or sugar; 1035; acid; amorphous urates.
2-7	*b*	98	77	5,040,000	27,120	88.8% 24,083	5.4% 1,464	.8% 217	5% 1,356	....	First count after operation; drainage.
2-8	*c*	100.6	72	4,710,000	20,400	76.6% 15,626	12.6% 2,570	2.2% 449	8.6% 1,755	....	Fluids taken, fl. oz. xxxiii; urine voided, fl. oz ix; stools, i.
2-9	*d*	99.4	74	4,930,000	17,760	76% 13,498	13.8% 2,451	2% 355	8.2% 1,456	....	Fluids taken, fl. oz xliv; urine voided, fl. oz. xvi; general condition excellent; no pain since operation.
2-10	*e*	98.8	70	4,730,000	16,160	66% 10,666	19.4% 3,135	2.4% 388	12.2% 1,971	....	
2-11	*f*	99	68	4,600,000	14,000	63.2% 8,848	19.8% 2,772	2.6% 364	13.8% 1,932	.6% 84	Dressed to-day; drainage removed; wound clean.
2-12	*g*	99	69	4,430,000	11,840	65.8% 7,791	21% 2,486	2.8% 331	9.6% 1,137	.8% 95	Condition good.
2-13	*h*	98.6	66	4,490,000	10,240	77% 7,885	14% 1,433	.8% 82	7.8% 799	.4% 41	
2-14	*i*	97.8	66	4,210,000	9,600	74.8% 7,181	16.2% 1,555	1.6% 154	7.4% 710	....	

CASE 21.—Mr. H., Myxo-Sarcoma of Parotid.

Date.	No. Counts.	Temperature.	Hemoglobin.	Erythrocytes.	Leukocytes.	Polymorpho-nuclear.	Lymphocytes.	Mononuclear.	Transitional.	Eosinophiles.	Remarks.
4–11	a	99.1	86	5,990,000	13,840	66% 9,135	20.4% 2,823	2% 277	4.8% 664	6.8% 941	
4–11	b	97.3	89	5,830,000	21,360	90% 19,224	5.4% 1,154	.8% 170	3.4% 726	.4% 85	First count after operation.
4–12	c	99	85	6,200,000	16,000	72.6% 11,616	17% 2,720	2.2% 352	5.8% 928	2.4% 384	Fluids taken, fl. oz. xxiv; urine voided, fl. oz. xii+; stools, i.
4–13	d	98	84	5,880,000	14,560	64.17% 9,343	16.33% 2,378	2.67% 389	9% 1,310	7.83% 1,140	Soft diet; urine voided, fl. oz. xii+; stools, i.
4–14	e	98.1	81	5,520,000	14,000	67.4% 9,436	18.8% 2,632	1.6% 224	5.6% 784	6.6% 924	Full diet; urine voided, fl. oz. xxii+; stools, i; Comfortable.
4–15	f	98.4	79	5,500,000	9,760	66.6% 6,500	18.2% 1,776	1.8% 176	6.6% 644	6.8% 664	Full diet; urine voided, fl. oz. xliv.
4–16	g	98.3	82	5,410,000	12,640	78.4% 9,911	10.2% 1,289	.6% 76	4.2% 531	6.6% 834	Wound dressed; tube removed, and gauze inserted; clean.
4–17	h	98.1	78	5,270,000	10,080	64% 6,451	21.6% 2,177	1.4% 141	5.6% 565	7.4% 746	

CASE 22.—Mr. R., Ununited Fracture of Tibia (Bones United by Gimlet).

Date.	No. Counts.	Temperature.	Hemoglobin.	Erythrocytes.	Leukocytes.	Polymorpho-nuclear.	Lymphocytes.	Mononuclear.	Transitional.	Eosinophiles.	Remarks.
4–12	a	98.6	87	6,180,000	10,480	65% 6,812	26.4% 2,767	1.4% 147	6.6% 691	.6% 63	
4–12	b	97.4	80	5,590,000	28,240	89% 25,134	5.8% 1,638	1.2% 339	3.8% 1,073	.2% 56	First count after operation.
4–13	c	99.2	88	6,000,000	19,280	75.4% 14,538	13% 2,506	2.2% 424	9.4% 1,812	....	Considerable burning pain at site of wound; backache.
4–14	d	98.8	84	6,050,000	17,600	71.4% 12,566	16.8% 2,957	2.2% 387	8.6% 1,514	1% 176	
4–15	e	98.6	81	5,760,000	11,520	61.6% 7,096	22% 2,535	2.2% 253	7.8% 899	6.4% 737	Fairly comfortable; slight intermittent pain in leg.
4–16	f	99	80	5,510,000	10,720	60% 6,432	20% 2,144	1.8% 193	8.8% 943	9.4% 1,008	Comfortable; slept well.
4–17	g	98.4	84	5,690,000	11,280	63.2% 7,129	19.8% 2,234	1.2% 135	5.8% 654	10% 1,128	Slight stinging pain in leg.
4–18	h	98.6	80	5,500,000	12,800	71.2% 9,114	14.4% 1,843	.4% 51	4.2% 538	9.8% 1,254	Dressed to-day; *iodoform dermatitis;* wound clean.
4–19	i	98.6	81	5,510,000	13,920	74% 10,301	14.8% 2,060	1.2% 167	4.6% 640	5.4% 752	Dressed after count; wound clean; slight pain.

CASE 23.—Mr. T., Ununited Fracture of Both Bones of Forearm (Bones United by Halsted Splint).

Date.	No. Counts.	Temperature.	Hemoglobin.	Erythrocytes.	Leukocytes.	Polymorpho-nuclear.	Lymphocytes.	Mononuclear.	Transitional.	Eosinophiles.	Remarks.
11–20	a	98.8	74	5,550,000	10,800	65.8% 7,106	22.6% 2,441	2.6% 281	4.8% 518	4.2% 454	
11–21	b	98.6	73	5,710,000	11,200	68.2% 7,639	21.2% 2,374	2% 224	4% 448	4.6% 515	Urine: Amber; slightly cloudy; 1028; acid; no albumin or sugar.
11–22	c	98.6	74	5,390,000	9,040	61.29% 5,540	22% 1,989	2.43% 220	6.57% 594	7.71% 697	
11–23	d	97.4	80	5,840,000	27,600	93.2% 25,723	4.2% 1,159	.2% 55	2.1% 580	.3% 83	First count after operation.
11–24	e	100.8	76	6,060,000	18,240	79.5% 14,501	11.7% 2,134	2.3% 420	5.2% 948	1.3% 237	Has had considerable pain at site of wound. fluids taken, fl. oz. xxix; urine voided, fl. oz; xvi.
11–25	f	100.1	84	5,460,000	16,880	77.2% 13,031	12% 2,026	2.2% 371	6.2% 1,047	2.4% 405	Patient fairly comfortable, but slight pain in arm; fluids taken, fl. oz. xlii; urine voided, fl. oz. xviii; stools, iii.
11–26	g	100.2	75	5,520,000	12,960	70% 9,072	16.2% 2,100	2.4% 311	6.6% 855	4.8% 622	
11–27	h	99.4	79	5,730,000	12,400	70.4% 8,730	15.8% 1,959	1.6% 198	5.4% 670	6.8% 843	Comfortable.
11–28	i	100.8	81	5,340,000	18,000	83% 14,940	7.71% 1,388	1.57% 282	5.86% 1,055	1.86% 335	Owing to supposed slipping of Halsted splint and displacing of fragments, wound was opened on 29th, and pus was found.

CASE 24.—Tubercular Arthritis of Knee (Amputation of Thigh).

Date.	No. Counts.	Temperature.	Hemoglobin.	Erythrocytes.	Leukocytes.	Polymorphonuclear.	Lymphocytes.	Mononuclear.	Transitional.	Eosinophiles.	Remarks.
5–9	*a*	99	73	5,750,000	10,160	64.4% 6,543	21.4% 2,174	.6% 61	8.4% 854	5.2% 528	Urine: Yellow; cloudy; acid; 1028; no albumin or sugar; uric acid.
5–9	*b*	97.2	77	5,870,000	20,960	83.4% 17,481	8% 1,677	1.6% 335	6.6% 1,383	.4% 84	First count after operation; drainage.
5–10	*c*	99.6	69	5,730,000	12,960	73.2% 9,487	13.6% 1,763	2.2% 285	8.6% 1,114	2.4% 311	Fluids taken, fl. oz. xxx; urine voided, fl. oz. xvi; has slight pain.
5–11	*d*	99	74	5,500,000	13,360	70.2% 9,379	17.8% 2,378	1.2% 160	7.4% 989	3.4% 454	Fluids taken, xlv; urine voided, fl. oz. xviii; stools, iii.
5–12	*e*	98.4	78	5,740,000	11,120	60.6% 6,739	20.6% 2,291	1.6% 178	9.8% 1,090	7.4% 822	Fluids taken, fl. oz. lii; urine voided, fl. oz. xxxii; stools, i; dressing changed owing to oozing.
5–13	*f*	98.8	76	5,660,000	10,800	63% 6,804	19% 2,052	1% 108	9% 972	8% 864	Patient comfortable.
5–14	*g*	98.4	73	5,600,000	9,920	70% 6,944	16.8% 1,677	.4% 40	5.6% 555	7.2% 714	

CASE 25.—Mr. Q., Gonorrheal Arthritis (Incision and Drainage of Knee Joint).

Date.	No. Counts.	Temperature.	Hemoglobin.	Erythrocytes.	Leukocytes.	Polymorphonuclear.	Lymphocytes.	Mononuclear.	Transitional.	Eosinophiles.	Remarks.
1–20	*a*	99.4	62	4,175,000	14,480	76.8% 11,121	12.6% 1 ,824	3% 434	6% 869	1.6% 232	Fluids taken, fl. oz. xxvii; urine voided, fl. oz. xxv. Urine: Dark amber; neutral; slightly cloudy; 1020; no albumin or sugar.
1–21	*b*	100	68	4,060,000	17,400	74.8% 13,165	12.4% 2,182	4.2% 739	8.6% 1,514	....	First count after operation.
1–22	*c*	99.8	65	4,550,000	15.760	72.4% 11,410	14.8% 2,333	4% 630	8.6% 1,355	.2% 32	Fluids taken, fl. oz. xxxvi; urine voided, fl. oz. xii+; stools, i.
1–23	*d*	98.4	65	4,790,000	13,680	71.6% 9,795	16.2% 2,216	2.6% 356	8.4% 1,149	1.2% 164	Fluids taken, fl. oz. xlii; urine voided, fl. oz. xxviii; stools, i; dressed and joint irrigated.
1–24	*e*	99.6	64	4,610,000	13,200	72.8% 9,610	14.4% 1,901	3% 396	8.2% 1,082	1.6% 211	Complains of but little pain; edema about joint not so marked.
1–25	*f*	100.4	60	4,440,000	13,600	77.8% 10,581	11.3% 1,537	2.7% 367	6% 816	2.2% 299	Dressed and joint irrigated.
1–26	*g*	100.8	59	4,270,000	15,840	79.4% 12,577	12.4% 1,964	2% 317	4.2% 665	2% 317	

CASE 26.—Mr. G., Renal Calculus (Operation).

Date.	No. Counts.	Temperature.	Hemoglobin.	Erythrocytes.	Leukocytes.	Polymorphonuclear.	Lymphocytes.	Mononuclear.	Transitional.	Eosinophiles.	Remarks.
2–28	*a*	97	96	5,670,000	9,840	68.8% 6,770	20.4% 2,007	2.2% 216	8.4% 827	.2% 20	Urine: Yellow; clear; alkaline; 1025; no albumin or sugar; phosphates.
2–28	*b*	99.8	93	5,860,000	20,560	80.6% 16,571	13.2% 2,714	.4% 82	5.8% 1,193	....	First count after operation; vomited fl. oz. iv.
3–1	*c*	100.6	93	5,640,000	32,880	86.4% 28,408	4.6% 1,513	1.6% 526	7.4% 2,433	....	Fluids taken, fl. oz. liv; urine voided, fl. oz. xxvi; Urine: Amber; acid; albumin ⅛; no sugar; red and white cells; dark, narrow, granular casts; dressing this a. m. soaked with blood and urine.
3–2	*d*	98.6	86	5,770,000	26,640	89% 23,710	5.2% 1,385	.6% 160	5.2% 1,385	....	Fluids taken, fl. oz. lxxiv; urine voided, fl. oz. xxviii; stools, ii; considerable blood in urine.
3–3	*e*	99.2	86	5,120,000	16,240	86.8% 14,096	7.8% 1,267	.2% 33	4.6% 747	.6% 97	Fluids taken, fl. oz. lxxviii; urine voided, fl. oz. xxxvi; blood in urine slightly visible to eye.
3–4	*f*	99.6	85	5,480,000	14,880	83% 12,350	8.8% 1,310	.6% 89	7% 1,042	.6% 89	Fluids taken, fl. oz. lxxxiii; urine voided, fl. oz. xxxix; dressing removed to-day; packing removed from kidney; no flush about wound.
3–5	*g*	100	82	5,100,000	15,920	83.4% 13,277	7.2% 1,146	2% 319	5.8% 923	1.6% 255	Fluid taken, fl. oz. lxxxiv; urine voided, fl. oz. xxiii; dressed before count. Urine: Amber; cloudy; acid; 1020; floculent precipitate; mucus; trace albumin; no sugar; phosphates; blood cells; blood casts; uric acid crystals.
3–6	*h*	100.2	84	5,100,000	16,000	82.67% 13,227	8.67% 1,387	1.16% 186	6.5% 1,040	1% 160	Fluids taken, fl. oz. cii; urine voided, fl. oz. lviii; stools, ii.
3–7	*i*	99.6	82	4,850,000	13,280	71.4% 9,482	14.8% 1,965	2.4% 319	10.2% 1,355	1.2% 159	Fluids taken, fl. oz. cxiv; urine voided, fl. oz. xli; stools, ii. Urine: port wine; heavy sediment; acid; 1015; albumin ⅛; blood cells; amorphous uaters.
3–8	*j*	100	81	4,920,000	11,600	81.4% 9,443	9.8% 1,137	.4% 46	7% 812	1.4% 162	Fluids taken, fl. oz. cxvi; urine voided, fl. oz. lxi.
3–9	*k*	99.6	80	4,720.000	15,040	78.4% 11,791	12% 1,805	1.2% 180	6.8% 1,023	1.6% 241	Wound dressed to-day; pus.
3–14	*l*	99.4	83	4,550,000	19,760						

CASE 27.—Mr. L., Recurrent Epithelioma (Removal of Portion of Submaxillary Gland).

Date.	No. Counts.	Temperature.	Hemoglobin.	Erythrocytes.	Leukocytes.	Polymorpho-nuclear.	Lymphocytes.	Mononuclear.	Transitional.	Eosinophiles.	Remarks.
5–18	*a*	98.6	80	5,530,000	8,240	65% 5,356	25.2% 2,077	.4% 33	6.4% 527	3% 247	
5–18	*b*	97.8	81	5,660,000	16,960	92.2% 15,637	5.6% 950	....	2.2% 373	....	First count after operation.
5–19	*c*	100.4	83	5,670,000	13,720	73.4% 10,070	17.8% 2,442	1.4% 192	7% 961	.4% 55	
5–20	*d*	99.8	76	5,950,000	12,880	83.2% 10,716	11.8% 1,520	.6% 77	4.2% 541	.2% 26	Patient comfortable.
5–21	*e*	99.8	79	5,790,000	11,200	67.6% 7,571	20.8% 2,330	2.2% 246	6.4% 717	3% 336	
5–22	*f*	99.6	80	5,540,000	8,480	66.8% 5,665	21.6% 1,832	1.8% 152	6% 509	3.8% 322	Comfortable; no unfavorable symptoms.

CASE 28.—Mr. P., Epithelioma of Lip (Excision).

3–22	*a*	98.6	90	5,600,000	9,440	65.4% 6,174	20.2% 1,907	1.8% 170	7.2% 679	5.4% 510	
3–22	*b*	97.6	92	5,420,000	12,480	80.4% 10,034	13% 1,622	.6% 75	5.2% 649	.8% 100	First count after operation.
3–23	*c*	99	89	5,650,000	16,960	66.2% 11,228	21.4% 3,629	1.2% 204	6.4% 1,085	4.8% 814	Fluids taken, fl. oz. xxxii; urine voided, fl. oz. xxvi.
3–24	*d*	98.6	91	5,710,000	13,680	68.4% 9,357	21.4% 2,928	.4% 55	5.6% 766	4.2% 574	Fluids taken, fl. oz. l; urine voided, fl. oz. xxxii; stools, i; dressed to-day; wound clean.
3–25	*e*	98	86	5,320,000	11,520	59% 6,797	29.4% 3,387	1.4% 161	6.6% 760	3.6% 415	Patient quite comfortable.
3–26	*f*	98.4	90	5,560,000	10,240	66.6% 6,820	23.2% 2,376	1% 102	5.6% 573	3.6% 369	Union by first intention.

CASE 29.—Miss B., Lipoma of Neck.

11–9	*a*	98	81	4,970,000	7,920	53.5% 4,237	30.5% 2,416	4.5% 356	9.25% 733	2.25% 178	
11–9	*b*	98.8	83	5,640,000	13,760	81.86% 11,264	9.69% 1,333	2.68% 369	5.31% 731	.46% 63	First count after operation; vomited fl. oz. iii.
11–10	*c*	100.4	76	5,280,000	14,480	82.25% 11,910	10.25% 1,484	1.5% 217	5.5% 797	.5% 72	Fluids taken, fl. oz. xliv; urine voided, fl. oz. x+; stools, vi.
11–11	*d*	100.6	82	5,610,000	13,360	85.2% 11,383	8% 1,069	2.4% 320	4.2% 561	.2% 27	Fluids taken, fl. oz. lx; stools, i.
11–13	*e*	99.4	83	5,300,000	9,920	66.8% 6,627	21% 2,083	1.5% 149	7.2% 714	3.5% 347	

CASE 30.—Mr. F., Fracture of Patella (Barker's Operation).

11–14	*a*	98	85	4,920,000	13.840	68% 9,411	23.4% 3,239	3% 415	5.2% 720	.4% 55	Urine: Amber; clear; acid; 1022; no albumin or sugar.
11–15	*b*	98.2	80	5,270,000	14,480	79.6% 11,526	13.2% 1,911	1.6% 232	5% 724	.6% 87	
11–15	*c*	98.8	86	5,860,000	17,920	76% 13,619	15% 2,688	2.5% 448	6.5% 1,165	....	First count after operation; vomited fl. oz. iii.
11–16	*d*	99.4	81	5,380,000	14,800	78.1% 11,559	11.6% 1,717	3.7% 548	6.5% 962	.1% 14	Fluids taken, fl. oz. xlviii; urine voided, fl. oz. xlii.
11–17	*e*	99.4	79	5,730,000	13,920	72.6% 10,106	14.6% 2,032	2.6% 362	9.6% 1,336	.6% 84	Patient quite comfortable.
11–18	*f*	99.2	77	5,110,000	13,040	76% 9,910	16.7% 2,178	.3% 39	6.7% 874	.3% 39	

CASE 31.—MR. W., TRAUMATIC TALIPES EQUINO-VARUS (AMPUTATION OF TOE, AND TENOTOMY).

Date.	No. Counts.	Temperature.	Hemoglobin.	Erythrocytes.	Leukocytes.	Polymorpho-nuclear.	Lymphocytes.	Mononuclear.	Transitional.	Eosinophiles.	Remarks.
3-14	*a*	98	85	6,060,000	13,520	64.8% 8,761	24.6% 3,326	1.4% 189	7.4% 1,001	1.8% 243	Urine: Amber; cloudy; acid; 1026; no albumin or sugar; amorphous urates.
3-14	*b*	97.4	87	6,180,000	24,880	86.4% 21,496	11.2% 2,787	.2% 50	2.2% 547	....	First count after operation; plaster cast.
3-15	*c*	99	89	5,780,000	20,720	81.8% 16,949	11.6% 2,403	.4% 83	5.8% 1,202	.4% 83	Feels comfortable, except for slight lumbar pains.
3-16	*d*	98.6	82	5,970,000	16,480	68.8% 11,338	19.6% 3,230	1.6% 264	7.2% 1,187	2.8% 461	
3-17	*e*	98.8	83	5,680,000	16,560	60% 9,936	24% 3,974	1% 166	9% 1,490	6% 994	
3-18	*f*	98.2	77	5,620,000	16,160	59.2% 9,567	24.4% 3,943	.4% 65	9.4% 1,519	6.6% 1,066	Comfortable.
3-19	*g*	98.8	81	5.730.000	16,720	59.2% 9,898	24.8% 4,147	1.8% 301	6.4% 1,070	7.8% 1,304	
3-20	*h*	98	77	5,580,000	14,640	60% 8,784	28.8% 4,216	.2% 29	7% 1,025	4% 586	Patient has shown no unfavorable subjective symptoms.
3-21	*i*	98.8	78	5,900,000	12,560	57% 7,159	29.3% 3,680	.7% 88	7% 879	6% 754	
3-22	*j*	98.6	76	5,300,000	12,160	58% 7,053	30% 3,648	1% 122	6% 730	5% 608	
3-23	*k*	98.6	77	5,650,000	18,400	62.4% 11,482	29% 5,336	.2% 37	4.8% 883	3.6% 662	
3-24	*l*	98.6	76	5,670,000	14,800	51.2% 7,578	36.6% 5,417	.8% 118	6.4% 947	5% 740	Examination of wounds shows slight infection.

CASE 32.—MR. R., VARICOCELE.

2-13	*a*	98.8	86	6,020,000	10,640	71.6% 7,618	19.6% 2,086	1.6% 170	6.4% 681	.8% 85	Fluids taken, fl. oz. xviii; stools, i. Urine: Amber; clear; 1020; acid; no albumin or sugar.
2-13	*b*	92.2	89	6,030,000	12,800	84.3% 10,790	10.1% 1,293	.7% 90	4.6% 589	.3% 38	First count after operation.
2-14	*c*	98.4	86	5,740,000	12,960	67.2% 8,709	15.6% 2,022	1.6% 207	12% 1,555	3.6% 467	Fluids taken, fl. oz. lvi; urine voided, fl. oz. xxiii.
2-15	*d*	98.4	87	5,950,000	11,760	71.2% 8,373	13.2% 1,552	1.2% 141	8.4% 988	6% 706	Light diet; urine voided, fl. oz. xvi; stools, ii.
2-16	*e*	98.2	82	5,980,000	11,440	67.4% 7,711	21% 2,402	1% 114	6.8% 778	3.8% 435	Light diet; urine voided, fl. oz. xxvi; stools, i.
2-17	*f*	99	86	5,640,000	12,400	52.4% 6,498	29% 3,596	2.6% 322	8% 992	8% 992	Patient has been quite comfortable since operation.
2-18	*g*	98.2	88	5,340,000	11,440	55.4% 6,338	27.8% 3,180	1.6% 183	7% 801	8.2% 938	
2-19	*h*	98.4	83	5,290,000	10,480	62% 6,498	20.2% 2,117	1.6% 167	7.8% 817	8.4% 830	Dressed to-day; wound clean.

CASE 33.—MR. H., VARICOSE VEINS OF LEG.

2-27	*a*	97	79	5,570,000	9,040	58% 5,243	30.33% 2,742	2% 181	7% 633	2.66% 241	Fluids taken, fl. oz. xxxiii; urine voided, fl. oz. xxxii; Urine: Heavy pink precipitate; acid; 1023; no albumin or sugar; amorphous urates.
2-27	*b*	98	82	5,260,000	11,200	84% 9,340	12.6% 1,401	.4% 45	2.4% 267	.6% 67	First count after operation.
2-28	*c*	98.1	83	5,170,000	18,800	68.2% 12,822	23% 4,324	2.4% 451	3.6% 677	2.8% 526	Light diet; urine voided, fl. oz. xxi+; stools, iii.
3-1	*d*	98.4	83	5,390,000	11,200	60.2% 6,743	24.6% 2,755	.6% 67	5% 560	9.6% 1,075	Light diet; urine voided, fl. oz. xxxiii; stools, i.
3-2	*e*	98.2	80	5,600,000	14,560	62.6% 9,114	21.6% 3,145	1.2% 175	5.2% 757	9.4% 1,369	Full diet; urine, fl. oz. xlviii; stools, ii.
3-3	*f*	98	80	5,400,000	10,720	59.2% 6,346	23.4% 2,508	1.4% 150	6.2% 665	9.8% 1,051	

CASE 34.—MR. G., CYSTITIS (CYSTOSCOPIC EXAMINATION).

Date.	No. Counts.	Temperature.	Hemoglobin.	Erythrocytes.	Leukocytes.	Polymorphonuclear;	Lymphocytes.	Mononuclear.	Transitional.	Eosinophiles.	Remarks.
3-1	*a*	98.6	81	5,300,000	11,840	64.6% 7,649	24% 2,842	.4% 47	4.8% 568	6.2% 734	
3-1	*b*	97.4	83	5,550,000	12,640	72.8% 9,202	20.4% 2,579	.4% 50	4% 506	2.4% 303	First count after ether.
3-2	*c*	98.8	82	5,700,000	11,760	65.8% 7,738	24% 2,822	1.4% 165	4.6% 541	4.2% 494	Fluids taken, fl. oz. xl; stools, i.

CASE 35.—MR. C., CYSTITIS (CYSTOSCOPIC EXAMINATION).

3-16	*a*	97.4	82	5,810,000	9,360	61.8% 5,785	25.2% 2,359	1.4% 131	9.8% 917	1.8% 168	Fluids taken, fl. oz. xxx; urine voided, fl. oz. xlviii; Urine: Amber; alkaline; 1017; trace of albumin; no sugar; pus and epithelial cells.
3-16	*b*	97.6	91	6,280,000	10,880	69.8% 7,594	19.4% 2,111	1.6% 174	8% 870	1.2% 131	First count after ether; amount of ether, fl. oz. xii; no vomiting.
3-17	*c*	98.2	90	6,220,000	10,160	64.2% 6,523	25% 2,540	1.4% 142	8.2% 833	1.2% 122	Fluids taken, fl. oz. xliii; urine voided, fl. oz. l; stools, i.
3-18	*d*	98.4	90	6,070,000	8,400	65% 5,460	23% 1,932	1% 84	9.3% 781	1.7% 43	

CASE 36.—MR. P., ANKYLOSIS SHOULDER (BREAKING UP ADHESIONS UNDER ETHER).

2-17	*a*	97.6	84	5,720,000	10,000	69% 6,900	19.8% 1,980	2% 200	9% 900	.2% 20	
2-17	*b*	97	84	5,910,000	16,000	85.2% 13,632	9.2% 1,472	1.0% 160	4.4% 704	.2% 32	First count after ether.
2-18	*c*	99.	79	5,880,000	14,880	69.2% 10,297	15.2% 2,262	2.4% 357	12.8% 1,905	.4% 59	Full diet; complains of considerable pain in shoulder.
2-19	*d*	98.4	81	5,440,000	12,400	63.8% 7,911	19.2% 2,381	1.8% 223	14.6% 1,810	.6% 75	Full diet.
2-20	*e*	99	85	5,360,000	10,240	68.2% 6,984	17% 1,741	1.8% 184	12% 1,229	1% 102	Full diet.
2-21	*f*	98.2	81	5,480,000	8,640	60.2% 5,201	22.8% 1,970	3% 259	12.8% 1,106	1.2% 104	Full diet.

CASE 37.—MR. B., CYSTITIS (CYSTOSCOPIC EXAMINATION).

4-5	*a*	98.2	92	5,950,000	10,800	74.6% 8,057	18.4% 1,987	1.4% 151	4.8% 519	.8% 86	Urine: Yellow; cloudy; acid; 1006; no albumin or sugar.
4-5	*b*	97.8	88	6,080,000	13,200	76.2% 10,058	14.5% 1,914	.8% 106	7.5% 990	1% 132	First count after ether; amount of ether used, fl. oz. viii.
4-6	*c*	99.4	91	5,820,000	14,560	73.4% 10,687	16.4% 2,388	1.4% 204	7.4% 1,077	1.4% 204	Complains of some distress in hypogastrium; fluids taken, fl. oz. xxxii; urine voided, fl. oz lix.
4-7	*d*	98.8	90	5,980,000	13,200	75.6% 9,979	16.6% 2,191	.6% 79	6% 792	1.2% 159	Fluids taken, fl. oz. xxxiv; urine voided, fl. oz. xxxiii.
4-8	*e*	98	86	5.900,000	13,360	71% 9,486	17% 2,271	1% 134	7% 935	4% 534	Fluids taken, fl. oz. xviii; light diet; urine voided, fl. oz. xli; stools, i.
4-9	*f*	98.2	87	5,600,000	11,680	69.8% 8,153	21% 2,453	1.8% 210	5.8% 677	1.6% 187	Fluids taken, fl. oz. xlvi; stools, i; urine voided, fl. oz. lxxiv.
4-10	*g*	99	84	6,050,000	11,840	70.8% 8,383	18% 2,131	1.8% 213	7.4% 876	2% 237	Fluids taken, fl. oz. li; stools, i; urine voided, fl. oz. liii.

CASE 38.—MR. B., ANKYLOSIS SHOULDER (ADHESIONS BROKEN UP UNDER ETHER).

Date.	No. Counts.	Temperature.	Hemoglobin.	Erythrocytes.	Leukocytes.	Polymorpho-nuclear.	Lymphocytes.	Mononuclear.	Transitional.	Eosinophiles.	Remarks.
1–18	*a*	97.6	78	5,420,000	8,160	66.2% 5,402	21.4% 1,746	2% 163	5.8% 473	4.6% 376	Fluids taken, fl. oz. xx; urine voided, fl. oz. iv+. Urine: Amber; acid; 1027; no albumin or sugar.
1–18	*b*	99	86	6,160,000	10,000	78.6% 7,860	16% 1,600	1% 100	3.8% 380	.6% 60	First count after ether.
1–19	*c*	98.6	76	5,470,000	7,840	61.4% 4,814	26.8% 2,101	1.4% 110	6% 470	4.4% 345	Full diet; urine voided, fl. oz. xxvi; stools, i; complains of considerable pain in shoulder.
1–20	*d*	98.4	75	5,270,000	10,240	68.2% 6,984	21.4% 2,191	1.2% 123	3.2% 328	6% 614	Full diet; urine voided, xxxii; stools, i.
1–21	*e*	98	78	5,630,000	9,760	62.4% 6,090	25% 2,440	2.8% 273	4.6% 449	5.2% 508	

CASE 39.—MRS. M., OLD SUBCORACOID DISLOCATION OF SHOULDER (ATTEMPTED REDUCTION UNDER ETHER).

3–21	*a*	98.2	82	5,380,000	8,880	67.8% 6,021	20.6% 1,829	2.6% 231	8% 710	1% 89	Urine: Amber; clear; acid; 1020; no albumin or sugar.
3–21	*b*	97.4	81	5,590,000	14,880	88.4% 13,154	4.8% 714	1.4% 208	5% 744	.4% 60	First count after ether; complains of much pain in shoulder.
3–22	*c*	99.6	81	5,280,000	13,680	83.4% 11,409	8.8% 1,204	.4% 55	6.6% 903	.8% 109	Considerable pain in shoulder.
3–23	*d*	98.8	83	5,630,000	14,560	74.6% 10,862	14.6% 2,126	1% 145	8.6% 1,252	1.2% 175	Patient still complains of much pain.

Further counts refused.

CASE 40.—MR. R., RHIZOMELIC SPONDYLOSIS (EXAMINATION UNDER ETHER).

1–31	*a*	98.6	83	5,060,000	7,920	73% 5,782	20% 1,584	.8% 63	5.4% 428	.8% 63	
2–1	*b*	98	84	5,290,000	8,800	77.83% 6,849	16.17% 1,423	1% 88	4.83% 425	.17% 15	
2–1	*c*	98	86	5,060,000	17,280	93.8% 16,209	4.2% 726	.4% 69	1.6% 276	....	First count after ether; amount of ether used, fl. oz. xi.
2–2	*d*	99	84	5,160,000	11,600	75.8% 8,793	17.6% 2,042	1.2% 139	5.2% 603	.2% 23	Fluids taken, fl. oz. xxiv; urine voided, fl. oz. xv.
2–3	*e*	98.8	80	4,890,000	10,000	78.8% 7,880	12.6% 1,260	2.4% 240	4.8% 480	1.4% 140	Fluids taken, fl. oz. xxxvi; urine voided, fl. oz. xxi; stools, i.
2–4	*f*	98.2	79	5,070,000	9,120	73.2% 6,676	22.8% 2,079	.4% 37	3.2% 292	.4% 36	Light diet.
2–5	*g*	98.6	78	5,310,000	10,320	73.4% 7,575	18% 1,858	2% 206	6% 619	.6% 62	
2–6	*h*	98.6	75	4,800,000	8,080	68.2% 5,510	24% 1,939	.8% 65	6.2% 501	.8% 65	

MYOSITIS FIBROSA.

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(From the service of Charles H. Frazier, M. D., University Hospital; and from the William Pepper Laboratory of Clinical Medicine, Phoebe A. Hearst Foundation.)

Fibrous myositis of the skeletal muscles is itself a comparatively rare affection, and the cases in which the diagnosis has been confirmed by subsequent histologic study of a specimen are, indeed, extremely few. For these reasons, therefore, one feels warranted in placing on record the report of a case which exhibited in such a typical manner the pathologic and clinical manifestations of this affection.

Fibrous myositis seems to have been first recognized in the sternocleidomastoid muscle in torticollis, and in the great majority of the cases reported up to the present time, this particular muscle was affected. The entire number of recorded cases in which the diagnosis is confirmed by microscopic examination is very small. In a review of the literature one is impressed by the scarcity of reference to this condition in the writings of American and English pathologists and surgeons. While the histologic nature of the lesion seems now to be well established, and its symptomatology more clearly understood, its etiology is still a matter of conjecture.

I am indebted for much of the information I have acquired upon the subject to Lorenz who, in his monograph "Die Muskelerkrankungen," gives by far the most complete description of this lesion.

Etiology.—Myositis fibrosa may be divided according to its etiology into two groups: Primary or idiopathic, and secondary. Several theories have been advanced to explain the origin of the primary form: (1) Kader[2] believes it to be due to an infection by pathogenic microorganisms, and regards it as an attenuated or chronic form of that process active in the production of acute myositis; (2) König[3] holds that it is due to a constitutional anomaly whereby the affected individual exhibits a peculiar tendency to the production of connective tissue. Of these two theories, Lorenz favors the latter.

The secondary form may, from the etiologic standpoint, be divided into six groups:

(1) *Those due to trauma.* It has been observed in contusions and lacerations of the muscle, with or without the formation of a hematoma. The repair of the defect usually takes place through the medium of regenerated muscle tissue. Certain conditions may exist, however, which either interfere with muscle regeneration or excite the production of connective tissue. These conditions are associated most commonly with the reactionary processes which accompany trauma, particularly when the latter is repeated or when during the process of repair the muscle is not at rest. The hematoma which develops at the site of a rupture of the sternocleidomastoid muscle has been assignee by a number of writers as the predisposing cause of many cases of torticollis, and the multiple muscle ruptures attending chronic tenanus, according to de Brun, account in a certain number of cases for the development of this pathologic condition. (2) Those due to ischemic disturbances in degenerated muscle. (3) Those cases developing at the site of previously existing abscesses. (4) Those cases developing as sequellæ of non-suppurating forms of myositis; as the rheumatic, syphilitic and gonorrheal. This lesion has been observed too in the neighbor-

hood of tissues infected with tuberculosis, actinomycosis; and occasionally in the chronic forms of polymyositis hemorrhagica. (5) Those cases due to the presence of trichinæ in the musculature. (6) Those cases occurring in conjunction with scleroderma.

Symptomatology.—The primary form though most frequently localized either to an individual muscle or group of muscles, may, as in cases reported by Lorenz[1], King[4], and others, be more widely distributed. The pathologic process is slow in its development and its course is essentially chronic, extending over a period of months or even years. The site of predilection may be said to be the lower extremity, the muscles of the thigh and leg being attacked with equal frequency. There is seldom any febrile reaction and there is little if any general constitutional disturbance. Spontaneous pain in the affected region is at times a conspicuous symptom and may be of so great intensity as to demand absolute rest. Nocturnal exacerbations have been reported in some cases.

Upon palpation one discovers an immovable firm tumor of woody hardness; the overlying skin is leathery, cannot be picked up in folds, and is stained a deep brown. The tumor feels like a compact fibrous mass, irregularly nodular and fairly well defined except in those cases in which the subcutaneous tissue immediately overlying the tumor has become infiltrated. The affected musculature is moderately tender to pressure. In the advanced stage of the disease the electric reactions are in some cases greatly diminished, in others unchanged. There may or may not be disturbance of thermic or tactile sensation of the overlying skin. Complications involving the nervous system, the bones or joints, are unknown.

The symptomatology of the *secondary* form differs from the primary chiefly in two particulars: First, in that there is a more widespread distribution of the process and, secondly, in that the disease is ushered in with a process which is essentially acute. Instances of this secondary variety are met with more commonly in cases of torticollis. If the opportunity is offered to observe the entire course of the disease, it would be noted that there are two distinct stages, the acute and chronic. In the acute stage an inflammatory exudate into the affected area can be demonstrated almost immediately after the onset of the disease or after the lapse of a few days, and the symptoms are those of an acute myositis. The chronic stage gradually supervenes and is characterized by a substitution of muscle by fibrous tissue. The first clinical manifestation of this stage is a hardening of the affected muscle and a diminution of those subjective disturbances that mark the acute stage. There is less spontaneous pain, there is less tenderness on pressure, and the acute inflammatory phenomena in the surrounding tissues and in the overlying skin gradually subside. The indurated area diminishes and the muscle becomes attenuated and shortened. The subsequent contraction of the infiltrated muscle accounts for that interference with function which is such a conspicuous feature of the later stages of the disease. The active contractility and the electric reactions are either lost or very much impaired.

Diagnosis.—The diagnosis of either the primary or secondary form of fibrous myositis, based upon its clinical signs alone, is, to say the least, difficult and oftentimes impossible; a positive diagnosis can in many instances only be made by a histologic examination of the affected tissue. The conditions with which it is particularly liable to be confused are neoplasms, especially osteosarcomata, chronic osteomyelitis and osteoperiostitis, and other forms of polymyositis, especially the syphilitic.

Prognosis.—In spite of its long duration, the prognosis of this affection is usually favorable, the condition yielding to a prolonged course of treatment by massage and electricity. It should be borne in mind that occasionally the disease may recur and that it may be a forerunner of either a general or localized form of myositis ossificans. It is said that the affected tissue may undergo malignant change.

Treatment.—During the early period of the disease absolute rest of the affected muscles should be insisted upon, while during the later stages the presence or absence of pain on motion must govern one in his decision as to whether or not the use of the limbs should be interdicted. Operative intervention might be said to be indicated only in those cases in which the mass is causing sufficient pressure upon the adjacent nerve trunks to account for sensory or motor disturbances. Internal medication is practically of no avail in the treatment of this affection; mercury, the iodides and numerous other drugs have been employed without exhibiting any beneficial effect. The treatment yielding the best results is purely local. Massage and electricity together with the use of variously medicated baths seem to promote the absorption of a part, at least, of the fibrous tissue.

Pathologic Anatomy.—The macroscopic appearance of the tissue in *primary* fibrous myositis and the microscopic findings in excised sections of affected muscles have been described by Lorenz[1], Gies[5] Krukenberg[6], Lindner[7], Hackenbruch[8], Janicke[9] and other observers. The gross lesions are very marked. The indurated area, which grates on section with the knife, appears to the naked eye to be made up of almost white compact structure; in less advanced stages the affected structure consists of a groundwork of grayish-white tissue in which are seen reddish-yellow areas of muscular tissue, giving to a cross section a streaked appearance. The microscopic section shows in the earlier stages a broadening of the interstitial spaces which are occupied by a form of connective tissue with an abundance of nuclei and a rich blood supply. This tissue surrounds the isolated and atrophic muscle bundles; the muscle fibres themselves show in some places evidences of degeneration and in others atrophic changes. The cross striations almost entirely disappear while the longitudinal are well marked. In the sarcolemma proliferation of the nuclei will be noticed and in the region of the blood-vessels there is a small round cell infiltration.

The pathologic anatomy of the *secondary* form does not materially differ from that of the idiopathic variety. It shows variation according to the position and stage of the disease. Best known and most studied are the indurations observed in the sternomastoid muscle. Here it is usual to find either the sternal or the clavicular portion of the muscle alone affected, although in about one-fourth of the reported cases the process involved the entire muscle. The affected muscle is, in the majority of cases, shortened and thinned, of a pale red to dirty gray color; on closer inspection can be seen islets of atrophic muscle surrounded by connective tissue. At times the diseased muscle is adherent to the adjacent structures; the neighboring glands may be enlarged.

In the microscopic picture the increase of the interstitial connective tissue is the conspicuous feature. In a longitudinal section the fibrous tissue is seen to run parallel to the muscle fibres and to force apart the muscle bundles. The number of muscle fibres is diminished in proportion to the increase of connective tissue. The individual muscle fibres in places appear narrowed but retain their normal protoplasm, while many of the fibres show cloudy swelling and vacuolation. Cross section shows the muscle fibres in groups or nests enclosed in broad masses of connective tissue and atrophied, apparently from pressure. Many normal and a few hypertrophied muscle fibres may be seen. The connective tissue is, in the early stage, rich in nuclei and blood-vessels and shows areas of small round cell infiltration, while in lesions of long standing it is more fibrous in character, contains fewer nuclei and is poorly supplied with blood-vessels.

The case which I wish to record is one of a man who recently came under the care of Dr. Charles H. Frazier, through whose courtesy I am permitted to make this report.

The patient, R. R., a miner by occupation, aged twenty-four years, has enjoyed good health for the greater part of his life, having had only two severe illnesses, scarlet fever and diphtheria, both of which occurred in his childhood. He has had an inguinal hernia for the past six years and during this same period has had rather frequent attacks of articular rheumatism, none of which have been very severe. No history of syphilis can be obtained. His family history is good; one distant relative died of tuberculosis.

On September 12, 1900, while working in a coal mine, he was struck on the outer side of the right thigh by a piece of coal, weighing about four pounds, which had fallen a distance of three feet. At the time of the impact the inner surface of the thigh was resting upon the ground. There was but little swelling or discoloration or other evidence of traumatism, although he suffered considerable pain which, at the end of a week, compelled him to stop working. He was treated at home for rheumatism, but as there was no improvement in the local condition after two weeks of treatment he sought admission in a hospital, where he remained under treatment for variously diagnosed conditions for ten weeks. It was at one time considered to be osteomyelitis and operative intervention was advised. During this period of thirteen weeks the lesion had become progressively worse. About December 1, he noticed a deeply situated nodule, which he describes as being quite hard and as large as a walnut, on the outer surface of the thigh; it was the seat of almost continuous pain. This nodule increased in size and the symptoms became more severe until his admission to the University Hospital, January 1, 1901, when his condition is described as follows:

A prominent swelling occupies the outer central portion of the right thigh. It is irregularly ovoid in shape, measures six inches longitudinally and four inches transversely, presents a uniform and marked degree of hardness and appears to be beneath the deep fascia and attached to the femur. The overlying skin is indurated, discolored and somewhat mottled in appearance, and is moderately adherent to the mass. Tenderness on pressure is limited to an area about an inch and a half in diameter near the centre of the tumor, which corresponds to the site of the original injury and to the position where the growth was first noticed. The extensor muscles of the thigh are somewhat atrophied. There is distinct limitation of motion in the knee joint. Pain is constantly present in the mass and is augmented by muscular action; at rest the pain is not severe, excepting at night, when it is paroxysmal in character and of sufficient intensity to disturb his sleep. The pain is referred from the tumor to the knee and leg. His general condition has not been materially affected; since the injury, probably as a result of confinement and inactivity, he has lost about fifteen pounds. The neighboring lymphatic glands are not enlarged. The shadow cast by the mass upon the skiagraphic plate was denser than that cast by the normal muscle, though not so dense as bone.

While the patient was under observation the possibility of the case being one of osteomyelitis, osteoperiostitis, osteosarcoma and a tumor of fibrous formation were considered and all but the two latter conditions excluded.

An exploratory operation was advised, and on January 26, the patient having given consent to an amputation at the hip joint in case any condition was found which would warrant such a procedure, the affected region was exposed, a longitudinal incision was made through the centre of the growth and down to the femur and sections from different regions of the affected muscles were removed for microscopic examination. The entire thickness of the quadriceps extensor muscle was firmer and paler than normal and evidently the seat of pathologic changes. To the naked eye it appeared as though narrow septa of fibrous tissue penetrated the muscle in different directions, but the muscle tissue was not replaced or displaced by any encapsulated growth. The deep fascia was thickened and formed a part of the new growth. No limiting capsule could be distinguished. The femur, to which the overlying structures were only moderately adherent, was normal in size and the periosteum unaltered. As there was nothing in the appearance of the lesion to suggest malignancy, the wound was closed without further surgical interference.

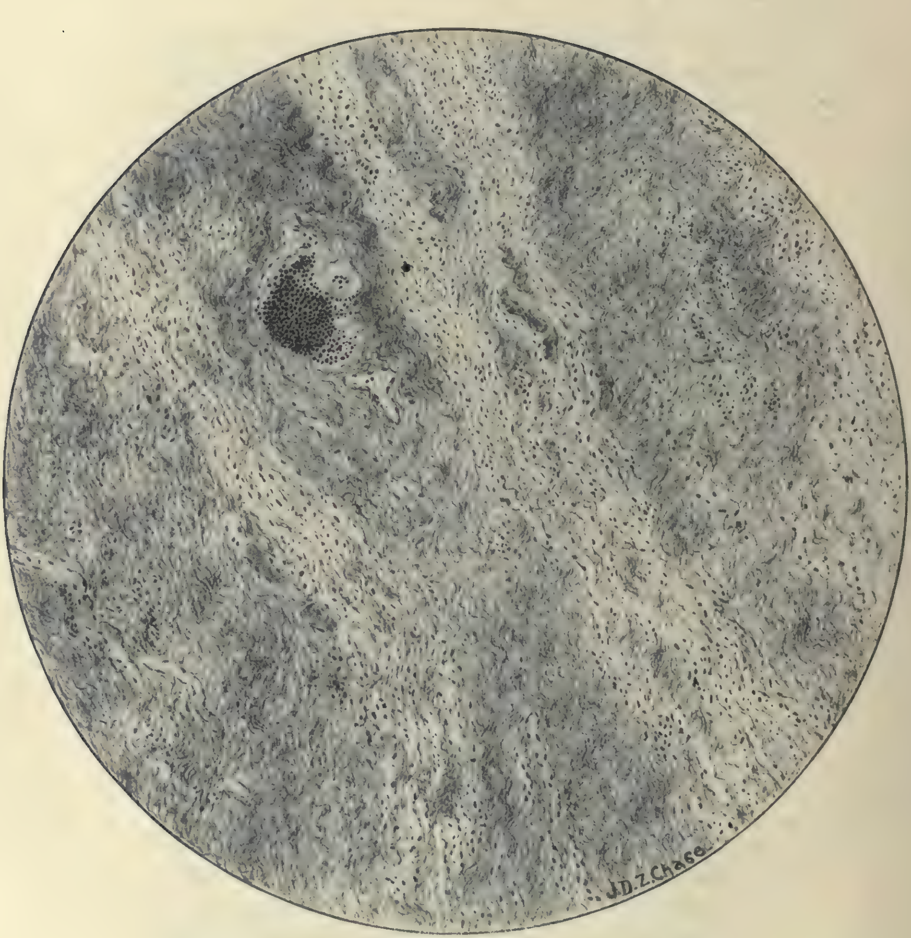

FIG. 1.—Myositis Fibrosa. Longitudinal section.

Pathologic Report.—The excised sections of tissue, seven in number, taken from different portions of the affected muscles, all present a practically similar histologic appearance. In longitudinal section the specimen is seen to be largely composed of fibrous connective tissue, which not only widely separates the muscle bundles, but has also extended into the endomysial spaces and by its proliferation in this position dissected up the individual fibres, many of which are entirely isolated and surrounded by broad bands of connective tissue. The connective tissue contains a small number of nuclei and is not richly supplied with blood-vessels. The muscle fibres themselves show great variation in size and appearance, and many are tortuous. The cross striations have disappeared in some fibres, while many retain their normal appearance. In certain areas the muscle fibres are atrophied, and in some places are undergoing degeneration. On cross section one sees the same predominance of connective tissue, particularly in the perimysial spaces, but the ingrowth between the individual muscle fibres is not so evident. The changes in the muscle fibres themselves are, however, more clearly demonstrated. In some regions an entire muscle bundle is composed of almost normal fibres, in others the bundles contain atrophic fibres, and again in others, and particularly in the periphery of the muscle bundles, the muscle fibres have undergone hyaline and other degenerative changes. A few show vacuolation and fissuring and an absence of nuclei. The blood-vessels are everywhere fully formed and for the most part normal, although in places the vessel walls are thickened. Only in the region of a few blood-vessels is there present a round cell infiltration.

Treatment.—In the case under discussion the treatment consisted at first of absolute rest and massage; later, while the massage was continued, the patient was allowed to get up and walk about the wards and corridor. Whether or not the treatment was responsible for the improvement that followed is difficult to say. The diminution of the constant pain, the cessation of paroxysmal pain, the reduction in size of the growth and restoration of function all gave evidence

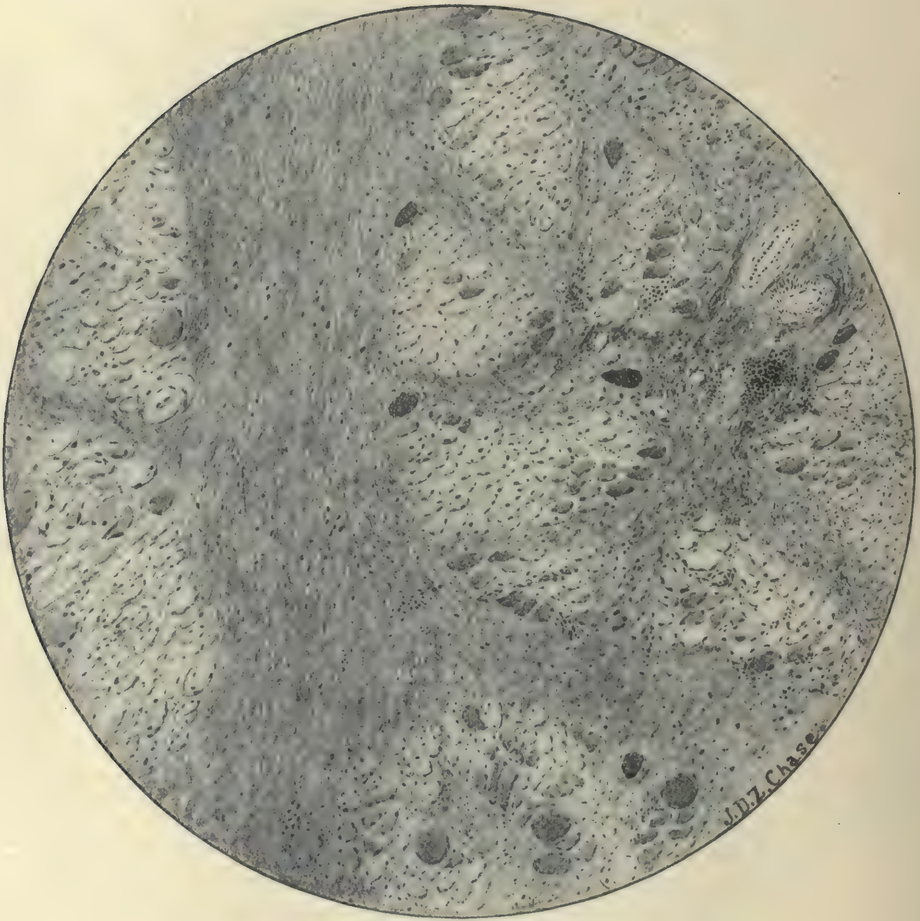

FIG. 2.—Myositis Fibrosa. Cross section.

of the favorable course the case was pursuing. At the time of writing the mass is about one-half its original size, is not tender to pressure and is painful only after long-continued use of the limb. Motion at the knee joint has been restored nearly to normal, and the case gives promise of an almost complete restoration of function. While the prognosis is, on the whole, favorable, this opinion should be expressed with some reservation, bearing in mind the possibility of an arrest of this process of resolution, of a calcareous infiltration, or of malignant change.

While the pathological findings as well as the clinical signs and symptoms of the reported case correspond quite accurately to the described idiopathic or primary form of fibrous myositis, the history would warrant one in designating it as a secondary form.

We will not consider the propriety of the previously recorded classification of fibrous myositis, nor discuss the merits of the various theories which have been advanced to account for its development, but will simply state our conclusions as to the probable etiology in this case.

The first element in its causation was the presence of that condition referred to by Konig, in which there is a tendency in the affected person to the production of connective tissue. The determining cause was trauma which by contusion and perhaps laceration of muscle tissue and interference with the blood and nerve supply, so reduced the vitality of the part that it was rendered possible for this anomalous predisposition to manifest itself. In the early stage the pathologic process was probably further influenced by constant irritation caused by continuous use of the affected muscles, while later, when the lesion had assumed demonstrable size, it, in itself, by pressure, irritation, and disturbance of circulation and nutrition, favored its own development.

The diagnosis in the reported case is supported by microscopic proof, the findings corresponding accurately to the accepted histologic anatomy of fibrous myositis.

A correct diagnosis was of particular importance in this case, inasmuch as had the growth been of a malignant nature, it would, because of its position and extent, have demanded amputation at the hip joint. It seems impossible to make a certain diagnosis without microscopic examination or, at least, a study of the macroscopic appearance of the lesion through an exploratory incision, and while one would not advocate indiscriminate operative interference, it seems reasonable to conclude that in many cases presenting the symptoms common to fibrous myositis and other lesions of a benign or malignant nature, an exploratory incision is not only justifiable but imperative.

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FURTHER STUDIES OF GRANULAR DEGENERATION OF THE ERYTHROCYTE.[1]

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In a previous communication, read at the meeting of the Association of American Physicians, held at Washington, April 29, 1901, and published in The American Journal of the Medical Sciences,[2] we presented our investigations of granular degeneration of the erythrocyte and in particular the facts bearing on the relations of this condition to lead poisoning. The material which we then accumulated gave us the opportunity to discuss the morphology of the condition and also its probable etiology. The direct dependence of the degeneration upon lead poisoning was shown by the regular occurrence of the granules in cases of lead poisoning admitted to the hospital, by the invariable discovery of the granules in men working in various capacities in lead works, by the discovery of granules soon after the administration of therapeutic doses in healthy individuals, and by the typical appearance of the corpuscles in dogs subjected to subacute or chronic lead poisoning. Further, we feel prepared to express a positive belief that the granular degeneration is the result of protoplasmic changes rather than the consequence of a nuclear fragmentation. We could see no relation between the granular condition and polychromatophilia excepting a frequent coincidence of the two conditions. Our belief was and remains that this granular condition is a true degeneration of an independent kind. We did not at that time feel prepared to state whether it occurs in lead poisoning as a result of the direct action of lead, or whether it is the consequence of anæmic conditions occasioned by the lead ; nor did we then arrive at any conclusion as to the place of origin of the changes found in the circulating erythrocyte. The present communication has for its purpose: in the first place a further discussion of the probable nature of the granules, and in the second place the report of some observations made to determine, if possible, the location in which the changes take place.

To determine the place of origin of the changes, we studied the blood taken from different parts of the circulation as well as scrapings and preparations from the bone marrow and splenic pulp. The material was taken from four animals that had been kept under the influence of lead for a considerable length of time. First, blood was taken from an artery and vein of the stomach, intestines, liver, spleen, and heart of etherized animals two hours after they had been given large doses of acetate of lead. The animals in each case had been under the influence of lead for some time, and granular erythrocytes were present in the circulating blood. The purpose of this experiment, which was prompted by Grawitz's view regarding the gastro-intestinal origin of the granular degeneration, was to determine whether erythrocytes showing this degeneration occur more abundantly in the blood of the portal vein and its tributary circulations than elsewhere. In only one of our experiments could we recognize an unequal distribution of granular cells. In this case more granular erythrocytes were found in the veins of the spleen, liver, and intestines than elsewhere. We, of course, cannot pretend that this single experience is of much weight in deciding the matter under discussion.

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[1] Read at the meeting of the American Medical Association, June. 1901.

[2] September, 1901.

The bone marrow and spleen were examined in two ways: (*a*) By preparing spreads made from scrapings of the cut surface of the organs, and (*b*) by embedding portions of the organs, hardened in various ways, in paraffin, and sectioning. In the spreads granular erythrocytes, both nucleated and non-nucleated, were easily demonstrated, but were not more abundant than in the circulating blood. Fixation by heat and in mixtures of ether and absolute alcohol and in absolute alcohol and 1 per cent. formol gave the best results, heat being by far the most satisfactory. The sections did not in any case show granular cells, as the red corpuscles were more or less crenated, whatever the method of fixation. We could not, therefore, be certain of the presence or absence of granular erythrocytes.

The result of these experiments then gave us no indications of the probable place of origin of the granular degeneration. In no instance did we find more abundant granular cells in the bone marrow or spleen than in the peripheral blood.

Some experiments seemed desirable to determine whether the granular cells existed in the circulating blood or whether, on the other hand, they are artefacts. The characters of the granules, the regularity of their occurrence in the blood in certain diseases, as well as their discovery in scrapings of tissues had convinced us that the granular corpuscles are not artefacts, and the question has not been seriously raised. Nevertheless, we thought it advisable to practice injection of certain stains to determine whether the fresh blood-corpuscles after such injections would show granular cells. Dogs that had been kept under the influence of lead until the blood showed granular erythrocytes in abundance were etherized, and solutions of methylene blue or neutral-roth in 0.8 per cent. NaCl solution were injected into a vein. Specimens of blood were taken at various intervals of time from the ear and examined fresh or after drying and fixation. The injections of methylene blue gave the only positive results. The blood in the successful cases showed nucleated and non-nucleated erythrocytes containing pale blue granules. The appearances of these granular cells were in every respect identical with those of the granular cells seen in stained spreads of the blood obtained before the injection of methylene blue, excepting that the staining of the granules was a little less intense. We could not confirm the observation of Sabrazes, Bourret, and Legér that the granules are eccentrically situated and show a tendency to extrusion.

The dried specimens of blood prepared as above described showed exactly similar conditions.

We have made a few attempts at artificial production of granular degeneration outside the body, and refer to them here, though we are aware of their unsatisfactory character. Quantities of human blood and of dog's blood were mixed with blood serum of dogs that had been under the influence of lead for some time. In no case did we reach positive results. The rapid disintegration of the red corpuscles under such circumstances naturally renders the experiment of little practical value. Equally unsatisfactory results attended the mixture of human blood and dog's blood with various solutions of acetate of lead. Sabrazes, Bourret, and Legér attempted to produce the degeneration by injecting solutions of lead into a ligated vein of a dog's leg, but without success.

A study of the various pathological conditions in which granular degeneration of the erythrocytes occurs seemed to us of possible importance in elucidating the question of the place of origin of the degeneration, and perhaps also its nature. Such a study is of course of even greater and more immediate interest in determining the diagnostic value of this reaction of lead poisoning. We therefore studied a considerable series of cases representing various diseases, and will refer to our results under the headings—chlorosis, pernicious anæmia, leukæmia, and miscellaneous medical and surgical diseases. The results obtained show that no explanation of the nature of the degeneration or its place of origin could be reached in this way.

CHLOROSIS. Contrary to the experience of other observers, we have found granular erythrocytes quite frequently in this disease. Among 18 cases examined by us there were 11 in which the granular cells were abundant. In 6 of the 11, the granules were fine; in the other 5 they were fine and occasionally coarse. In only 1 of the cases were the granules numerous. In this case the hæmoglobin was only reduced to 50 per cent., while in most of the cases a far greater reduction was noted. In all of the 11 cases polychromatic cells were seen, but these seemed to bear no relation in intensity or number to the granular cells.

PERNICIOUS ANÆMIA. Judging from the seven cases which we observed, and from the reports published by others, granular degeneration is a constant condition in advanced stages of pernicious anæmia. We found the granules fairly numerous and at times very large and conspicuous. Though, however, in the number and the character of the granules the blood of pernicious anæmia was usually distinguished from that of other diseases, we did not often find in pernicious anæmia the extraordinary number and variety of granules, coarse and fine, seen in nearly all of the cases of lead intoxication which we have examined; and the other characters of the blood would render a differentiation easy.

LEUKÆMIA. We examined ten cases of this disease and found granules in every one, though they were usually fine and not present in large numbers. We shall have occasion to refer again to this matter, as the occurrence of the granules in leukæmia is of particular importance in connection with the determination of the nature of granular degeneration, nucleated erythrocytes being so abundant in this disease and nuclear degenerations of all kinds so frequent. We should look then to this disease more than in any other for a confirmation of the view that granular degeneration results from fragmentations of the nucleus.

MISCELLANEOUS MEDICAL AND SURGICAL DISEASES. In addition to the 35 cases above referred to, we have examined the blood in 105 patients in the medical and surgical wards of the University Hospital, and have discovered granular erythrocytes in 34 of these cases. In the 34 cases the diagnoses were as follows: typhoid fever, 3 cases; valvular heart disease, 3; peritonitis, 3; septicæmia, 3; tuberculous arthritis, 2; malaria, 2, and pertussis, heart disease and nephritis, lobar pneumonia and pleurisy, phthisis, malignant endocarditis, aneurism and nephritis, nephritis and anæmia, splenic anæmia, secondary anæmia, pseudoleukæmia, chronic diarrhœa, phlyctenular conjunctivitis, orchitis, carcinoma of stomach, lymphoma of neck, sarcoma of neck, empyema, osteomyelitis, each 1 case.

Several observers have reported the discovery of granular red cells in cases of sepsis, and, though the direct bearing of septic infections upon the conditions has not been established, it is of interest to note that this condition was present in some of the cases enumerated above. Perhaps half of the above 34 cases were more or less septic. In the other half of the cases there was no such element, but the high grade of anæmia may have been alone operative in these. In several of the cases no clue whatever to the causation of the granules could be found. We might speak of them as accidental occurrences, but this would not serve as an explanation. In none of the 34 miscellaneous cases were the granules abundant or conspicuous. Two instances in which the blood picture approached that found in lead poisoning were a case of phlyctenular conjunctivitis in a boy, and a case of chronic diarrhœa in a man who had possibly taken acetate of lead in the treatment of his condition before he came under our observation. Even in these two cases we could easily distinguish the blood from that of lead poisoning, and in the remaining 32 cases the comparative sparseness of the granules and their finer character made the distinction very easy.

There were 71 cases in which we did not find granules. Some of these may be mentioned for the sake of showing that the classes of diseases in which the granules occur or do not occur give no indication of the probable source of the granular cells; and also to show that the condition of the blood as to infection or anæmia will not alone explain the degeneration.

We failed to find any granules in the following cases: 5 cases of valvular heart disease, 4 of phthisis, 4 of appendicitis, 7 of typhoid fever, 5 of sepsis, 6 of grippe, 3 of carcinoma of the stomach, 3 of diabetes, 2 of pneumonia, and in one case each of malaria, splenic anæmia, glanders, actinomycosis, and tetanus.

With the single exception of lead poisoning, no condition that we know of regularly causes this change, though other conditions operate to this end in occasional cases. As far as lead is concerned, we may refer again to our previous studies. In each of seven clinical cases of plumbism we found enormous numbers of the granular cells; and we may add six recent instances. In twenty-one men working in lead works, but showing no symptoms of lead poisoning, the granules were always found, but in varying numbers. Two of these men had worked in the lead works only four days. Moritz found the granular cells in six men working in lead works, but having no symptoms; and other observers, as Strauss, Grawitz, Behrendt, Sabrazes, Bourret, Legér, and Hamel (the last in 25 cases) found the granules in cases of lead poisoning. Strauss also discovered them in atropine poisoning and in rabbits and frogs poisoned with pyrodine. Kaminer and Rohnstein found granular cells in the blood of rabbits poisoned with phenylhydrazin on the fourteenth day of the intoxication. Sabrazes, Bourret, and Legér refer to a case of fatal copper poisoning in which numerous granules were found, but they failed to produce the degeneration in guinea-pigs by intraperitoneal injections of various toxic and non-toxic substances, such as distilled water, thallium acetate, carbonate of lithium, and sulphate of atropine, or by inhalations of nitrite of amyl, pyrodine, and phenyl hydrazin. Injections of lead acetate, however, caused the degeneration very rapidly in guinea-pigs as well as in rabbits. In our own experiments we have found the degenerations after poisoning a dog with potassium chlorate; the granules did not appear until shortly before death, but became very numerous. Another dog slowly intoxicated with corrosive sublimate showed only a few granules shortly before death. They were also present in large numbers in the blood of dogs kept under the influence of toxic doses of pyrodine for many days. It is evident, therefore, that toxic causes of various sorts are capable of producing the granular degeneration we are studying, but it is equally evident that no poison thus far studied is as regular in its production of the degeneration or as prompt in its action as is lead.

The discussion of the nature of the granular condition of the red corpuscles has divided observers into two groups: those holding that the granules originate from the nucleus, and those who regard them as the product of a specific degeneration of the protoplasm.

The former view was the one first put forward after the granular cells were recognized, and has been lately defended by Askanazy, Lazarus, Engel, Litten and Strauss. These authors look upon the granules as the result of nuclear fragmentation—karyorrhexis—and they believe that it is the means by which the nucleated cell normally loses its nucleus before becoming an adult cell and entering in the peripheral circulation. The attractiveness of this theory is largely dependent upon its adaptability as an explanation of the disappearance of the nucleus, a matter which has remained unsolved in spite of painstaking examinations of histologists; but more definite facts are required to establish the truthfulness of the theory. It would seem entirely reasonable to expect blood pictures showing a gradual transition from the state of normal nucleated cells to that of erythrocytes containing scattered granules, but without a nucleus. As a matter of fact, Litten claims that he has seen direct transitions from the normal nucleus to fully granular cells, both in the circulating blood and in the bone marrow, and he states that the nucleus gradually becomes paler as the granules increase in number and size. Somewhat similar statements are made by Ewing. Litten's observations were made in only one case, a rapidly fatal one of pernicious anæmia. Our own observations have included a large number of cases of intense anæmia and of various intoxications, both clinical and experimental, and we have found in these abundant granular cells in the circulating blood as well as in the bone marrow and other organs, but we have never in a single instance among the thousands of granular cells that we have carefully examined found the slightest suggestion of a nuclear fragmentation productive of granulations. We have repeatedly found and figured, from paintings by an artist and from photographs, associations of nuclei and granules, that is, we have recorded the occurrence of granules in nucleated cells; but in every instance the periphery of the nucleus has either been clear-cut as in the normal nucleated cell, and the chromatin of the nucleus has presented normal appearances, or when degeneration has been present there has been nothing suggesting even remotely an origin of granules in degeneration of the nucleus. The conditions in the blood of leukæmia seems to us to be particularly important in this connection. Nucleated erythrocytes with and without granules were very abundant in some of the cases studied, and in the same cases we often found evidences of nuclear degenerations, both in the white and in the red corpuscles. In no instance, however, could we see evidence of a transition of nucleated cells to granular cells.

If the theory of the gradual fragmentation of the nucleus were established, we should expect the evidences of such fragmentation to be most abundant in the bone marrow, where nucleated cells become non-nucleated; but our experience has been that the nucleated cells and the granular cells in bone marrow have been exactly the same as those of the peripheral circulation.

An observation made by us in several instances of still greater significance to disprove the nuclear origin of the granules was the discovery of karyomitosis in granular erythrocytes. One observation of this sort seems to us more valuable than any amount of negative evidence or of theorizing. It is unlikely that a nucleus could at the same time be in a state of active mitosis and of karyorrhexis.

The second theory regarding the nature of the degeneration, and the one to which we incline, is that which has been defended by Grawitz, Moritz, Hamel, and Bloch, and which attributes the granular condition to a peculiar protoplasmic degeneration. In the consideration of this theory we would first of all direct attention to the fact that all of the protoplasmic degenerations of erythrocytes that have been thus far described are characterized by the development of a basophilic tendency. Thus, in the studies of Maragliano and Castellino particular attention was directed to this peculiarity of the degenerated areas, and the behavior of polychromatophilic cells, so generally considered degenerative, is very similar. In no case is there the distinct basic affinity of the degenerated parts of the cell that is seen in the granular degeneration under consideration, but this is a point of too little importance to disprove our view.

Grawitz did not consider the granules the results of nuclear fragmentation, because in his earlier work he had not seen these granules in nucleated red corpuscles. He had expected to find them if these granulated cells were the unfinished red cells prematurely placed in the peripheral circulation. Under such circumstances granular nucleated red corpuscles should be found, or at least transitional forms should occur. Later he found nucleated erythrocytes with these granules in the protoplasm, but the nucleus was to all appearances normal. This last observation induced him to study the blood-forming organs, but here he was unable to see any evidence of these granules. From these observations he came to the conclusion that the granules are the result of degenerative processes in the hæmoglobin, caused by poisons acting directly upon the erythrocytes, and suggests that this takes place outside of the blood-forming organs.

Our own studies have shown granular nucleated erythrocytes in the peripheral blood, and also granular erythrocytes, nucleated and non-nucleated, in the bone marrow; but, like Grawitz, we have failed to find any transitions from the non-granular nucleated erythrocytes to the granular non-nucleated cell. While the proof of the protoplasmic origin of the granules is therefore more or less negative or indirect, we believe the evidence against the nuclear origin of the granules is direct and positive. This evidence may be summarized as follows:

1. Karolytic and karyorrhexic changes may be observed in nucleated red cells without showing any granular change in the protoplasm of the cells; on the other hand, granular degeneration may accompany these nuclear changes without association of the nuclear and granular processes.

2. The granulated red cells (coarse or fine granules) never show the remains or a suggestion of a former nucleus.

3. The granules are observed in karyokinetic red cells, and we have seen them associated with the several stages of the dividing nucleus. We cannot believe that such a progressive and retrogressive change can be present in the nucleus at the same time, without internal evidence of degeneration.

4. The very early appearance of these granules in the blood taken from the peripheral circulation (twenty-five hours after a dose of 7½ grains of the acetate of lead has been taken by one of us) to a certain extent indicates a probable beginning of the destructive changes in the erythrocytes (non-nucleated) of the peripheral blood, rather than in the erythrocytes (nucleated) at the moment in process of formation in blood-making organs.

5. The granules observed in the bone marrow were absolutely the same as those seen in the peripheral blood. Those in the nucleated cells, chiefly normoblasts, showed no evidence of derivation from the nucleus, the nuclei being in each case normal in size, shape, and staining qualities and like those of the neighboring nucleated cells which did not contain granules.

6. Finally it seems to us that in certain cases of leukæmia in which great numbers of nucleated red cells are always present, if these granules were nuclear derivatives, distinct steps or transitions could be demonstrated. Such is not the case. On the contrary, distinct degenerative changes, karyorrhexis, karyolysis, pyknosis, atrophy of the nucleus, etc., are present sometimes with and sometimes without granular protoplasm; but there are never in our experience any transitional stages to indicate gradual destruction of nuclei with liberation of substance that has gone to form granules. In addition very many of the nucleated cells showing nuclear degeneration contained no granules.

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SARCOMA OF THE LARGE INTESTINE.

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Most of the literature on sarcoma of the bowel and all of the statistical papers on the subject have appeared within the last twenty years. It is probable that, as in the case of sarcoma of other regions, notably of the mediastinum, many of the cases of this rare and interesting disease were classified as carcinomata before the era of accurate microscopical diagnosis. A number of papers on the subject have been published within the last two decades, in which the authors have gradually collected from the literature the scattered cases of this affection.

In 1883 A. Debrunner's[1] inaugural thesis was published at Zurich. In 1884 E. Pick[2] published his case. G. Newton Pitt,[3] in 1889, in a report of a case of lymphoid adenoma of the stomach and intestines, published abstracts of eighteen other cases. (These cases would be included by many pathologists under lymphosarcoma, and they are, therefore, referred to in this connection.) In 1890 Ludwig Orth,[4] in an inaugural dissertation, collected eleven cases of intestinal sarcoma, three of which were of the small and four of the large intestine, and four of the rectum.

M. Baltzer's[5] paper, which is so frequently referred to, and which was the most important and thorough study of the subject which had appeared up to that time (or, indeed, up to the present time, if we except the paper of Libman, recently published), appeared in 1892. He analyzed eleven cases from the literature and three cases occurring under his own observation in Madelung's clinic in Rostock. Smoler's[6] paper was published in 1898. Nothnagel[7] has a fairly comprehensive paper on the subject in his *System*, in the volume on diseases of the intestine and peritoneum, and Libman,[8] in his excellent article, which appeared in October, 1900, brings up to date the subject of sarcoma of the small intestine, collecting all the literature which he could find on that subject. In 1900 Blauel's[9] paper also appeared, entitled "Ueber Sarcome der Ileocecalgegend"—a collection of eight cases, including two of his own.

The operative side of the question of sarcoma of the bowel has been recently dealt with by Van Zwalenberg,[10] who has tabulated fifteen cases of resection of the bowel for sarcoma.

Of the above-mentioned papers Blauel's is the only one which pays especial attention to any portion of the large bowel. To avoid misunderstanding, however, it must be remembered that the subject of sarcoma of the rectum is not included in the above group. The rectum is the region of the bowel which is most frequently the seat of sarcoma. Clinically it can be well separated, as a rule, from what might more properly be regarded as internal sarcoma, and, according to Paneth[11] and Rosenheim,[12] it differs very little in its manifestations from carcinoma of the same region. We have, therefore, excluded it from our consideration.

The opportunity of studying a case of sarcoma of the ascending colon from a clinical and pathological stand-point having offered itself, we have deemed it of sufficient interest, in connection with a report of the case, to collect and analyze as many other cases of primary sarcoma of the cæcum and colon as possible. To this end we have availed ourselves of a number of cases reported in the list of contributions mentioned above, and collected sundry others from the literature at large.

The following is the history of our case:

John C., aged four years, was first seen at the surgical clinic of the Children's Hospital, March 19, 1900. He was referred from the medical clinic, where he had been under treatment for some time. His history was as follows:

Parents both living and in good health. Mother had been very sickly before this child was born. One other child, an older sister, living and well. The patient, a handsome, fair-haired boy, had no sickness of note until about a year ago. He had had an inguinal hernia for two and a half years. One year before, in 1899, while in England, he had been very ill, the exact nature of the malady being obscure, except that he presented a prominence of the abdomen (which is still present), and the physician told his mother that the liver was enlarged. For several months past he has suffered from dyspeptic symptoms, has been losing flesh, and is constipated at times. An examination of the patient showed him to be a rather anæmic child, of normal stature, and not much emaciated. The physical examination gave negative results, until the abdomen was reached. This was prominent, and palpation at once revealed the presence of a rather hard mass occupying the anterior median aspect, apparently filling up the umbilical and epigastric region, and, as far as could be determined, not continuous with either liver, spleen, or kidneys, there being a zone of resonance around it which separated it from the areas normally occupied by these organs. The mass gave the impression of being under or near the anterior abdominal wall, with no intestine separating or coming between them. There were no evidences of ascites.

The diagnosis lay apparently between a tuberculous peritonitis and some form of abdominal tumor. Dr. Samuel Ashhurst examined the case with us, and it was determined to put the child on medical treatment, with the possibility of the condition being a tuberculous one, and to keep him under observation for a time before proceeding to an operation. Inunctions of mercurial and belladonna ointments, equal parts, were ordered, with iron and cod-liver oil internally. The patient was not admitted to the hospital.

A few days later, March 26th, the patient developed a well-marked case of measles, which precluded all thoughts of operation for the time. The urine was examined and found to be negative, the only note being of the presence of abundant amorphous urates. Following the attack of measles, the distention of the abdomen became much greater. On April 1st it was noted that, owing to rigidity of the abdominal walls, the examination of the abdomen was unsatisfactory. There was resonance over the entire surface, and the xiphoid cartilage was pushed forward, protruding beneath the skin.

Following this date a febrile temperature developed, varying from 100.5° to 102.5°, and being highest in the evening. The tympanitic distention of the abdomen became so pronounced as to embarrass respiration, the abdominal walls being rigid, the veins dilated, the umbilicus pouting, but with no ascites. No obstruction of the bowels was present. Food seemed to cause discomfort, and there was evidently abdominal pain or at least discomfort at other times. Enemata of turpentine and the passage of a catheter were resorted to in order to relieve distention, and on April 8th the child passed, after an enema, a piece of fleshy tissue, about four inches long and less than half as wide, which resembled bowel wall, being thick, of fleshy consistence, and dark red in color. Under the microscope it seemed to be composed of fibrin, but, unfortunately, no careful histological examination of it was made.

Following this the temperature remained elevated for about two and one-half weeks, while emaciation became more and more marked, and the difficulty in feeding increased. The distention, which had been so extreme, became gradually reduced, being apparently lessened by the use of inunctions of mercurial and belladonna ointments and the application of a tight binder. The child was very peevish and resisted examination.

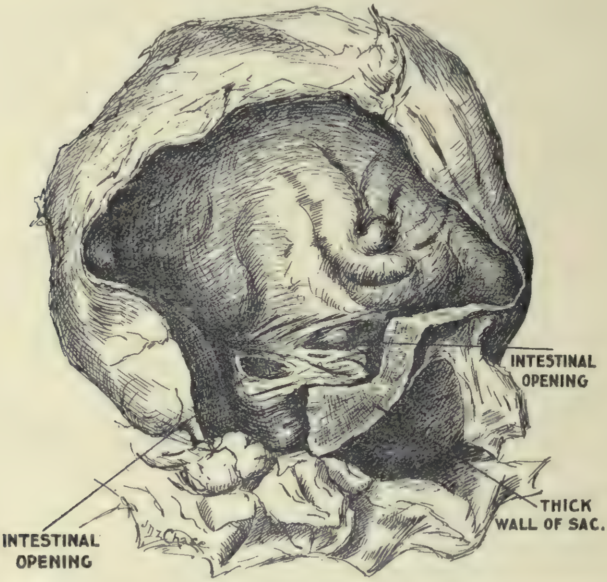
By May 5th the temperature had remained normal for some days, but weakness and emaciation were progressive. He had vomited a great deal for two or three days, and complained of pain at the nape of the neck. There was a somewhat troublesome cough, but no definite pulmonic signs. The bowels moved naturally. There was still some distention of the abdomen at the costal margin, but not much below this. The mass could be again distinctly outlined, but now in the right iliac region. The detection of the tumor had been impossible while the distention was so pronounced.

The child now refused almost all food and medicine. A few days later the left foot and leg became swollen and œdematous, and he developed what the mother described as convulsions—spells accompanied with crossing or rolling upward of the eyes, movements of the arms and legs, and followed by coma. Several of these occurred in the twenty-four hours. Examination of the urine showed only a small amount of albumin. Occasional movements of the bowels were noted. On May 14th, after having vomited everything for some days, and with no new symptoms, he died, apparently of asthenia, being emaciated to the last degree. At no time after the unfortunate attack of measles was he in condition to undergo laparotomy, which both the parents and ourselves looked forward to as offering a definite solution of the diagnosis, and perhaps some hope of relief.

Pathological Notes. The autopsy was performed twenty-four hours after death, and the following notes made:

The body is emaciated in the extreme. Rigor mortis is only partially developed. The left leg, foot, and thigh are moderately œdematous; no scars; slight discoloration in the dependent portions of the body. Incision in the median abdominal line reveals a very slight amount of subcutaneous fat. The incision opens up a cavity in the shape of a sac extending from above the umbilicus nearly to the symphysis pubis. Laterally it extends only slightly to the left of the median line, while on the right it reaches nearly to the anterior superior spine of the ilium. The walls of this sac are adherent to the anterior wall of the abdomen, and at this place are about 2 mm. in thickness. To the right and posteriorly they increase in thickness; the greatest thickness is about 2 cm., being at the posterior portion of the sac. The walls of the sac are composed of a yellowish-white, homogeneous tissue, of rather firm consistency, the external surface being mainly smooth, except in places here and there, especially posteriorly, where it is somewhat nodular. The inner surface is rather granular. The capacity of the sac is about one pint, and at the autopsy it contained about twelve ounces of a turbid, yellowish fluid, devoid of any special odor.

FIG. 1.



Sarcoma of the large intestine, showing aneurismal sac with the intestinal openings on the posterior wall.

On examining the inner surface of the sac the posterior wall is seen to present two openings, which correspond with the entrance and exit of the ascending colon. In the space between these two openings, which is about 5 cm. in length, no naked-eye vestiges of the former bowel can be found, the mucous membrane stopping rather abruptly on the surface of the thickened area at the openings of the bowel. Externally the sac is situated about 18 cm. above the ileocæcal valve, is pear-shaped, the base completely surrounding the ascending colon, and the apex pointing toward the median line. The only attachment of this sac to the parietal peritoneum is in the median line of the abdominal wall along the line of incision. After removal the sac measured 14 cm. in its vertical by 11 cm. in its transverse diameter.

The remainder of the peritoneal cavity in the immediate vicinity of the sac is free from adhesions. From the tumor, along the mesenteric attachments of the bowel, both above and below the sac, there is much infiltration, the mesentery being in places a full centimetre in thickness. The rest of the abdominal cavity seems quite free from involvement, excepting for a false diaphragm which stretches below the liver, stomach, and spleen, forming a separate cavity for these organs. There is an apparent perisplenitis and perihepatitis which attaches these organs to the diaphragm.

The spleen is not enlarged; the capsule is thickened and in places covered with a distinct yellowish-white exudate. The organ is firmly attached to the diaphragm by dense adhesions. On section the surface is brownish-red in color, and slightly fibroid in character.

The liver is greatly enlarged, of soft consistency, and of a bright yellow color. The outer surface is smooth, with the exception of several small areas which present a yellowish-white exudate, and in a few places it is adherent to the diaphragm. On section it is almost bloodless, and of the same bright yellow color throughout. The gall-bladder is normal.

The organs of the thoracic cavity are to all appearances normal, with the exception of one mediastinal lymph gland, which is distinctly enlarged, and on section is homogeneous, of a yellowish-white color, and of rather firm consistency. There is also a slightly enlarged lymph gland on the thoracic side of the right half of the diaphragm. The lungs show hypostatic congestion, but no evidence of tubercle or new growth.

The kidneys are very much enlarged, the left, which is the larger of the two, measuring 10 cm. in length by 5 cm. in width, and 4½ cm. in thickness. The capsule strips easily. They both present a slightly lobulated appearance, with irregular nodular prominences, of a yellowish-white color. The superficial vessels of the cortex stand out quite prominently on this yellowish-white background. On section the surface presents yellowish-white areas, especially prominent in the cortex; these areas are diffuse in places, and in other parts distinctly circumscribed. There are no areas of softening, and the bloodvessels, especially of the medulla, are prominent. There seems to be very little of the normal kidney substance remaining.

The suprarenal glands are not changed in appearance. The stomach appears normal. The small intestine is also normal. The cæcum and the appendix are infiltrated, especially along the mesenteric attachment, with a direct continuation of the growth. The retroperitoneal and mesenteric lymph glands are enlarged; some show the yellowish-white appearance so characteristic of the tumor mass, while others are red and soft.

The sac, with the cæcum and ascending colon, and a part of the ileum, were removed intact, as were also pieces of the liver, spleen, and left kidney, and much of the mesentery, and the enlarged retroperitoneal and mediastinal lymph glands. They were fixed with Müller solution, formol, etc., for further study.

Microscopical Examination. Sections were made from the thickest portion of the sac at its base; from its thin upper portion; from the posterior wall, including the afferent and efferent openings of the colon; from the appendix, and the lymphatic glands, peritoneal and mediastinal; from the spleen, the kidney, and the liver. Sections from the thickest portions of the sac are covered on the outer surface with peritoneum, and are composed of a reticular fibrous network, aggregated here and there into denser masses of connective tissue. The meshes of this framework are densely packed with small, round, mononuclear cells, the nuclei of which take the stain moderately well and show very distinctly a chromatin network, some also showing evidences of karyorrhexis, and here and there mitotic figures. Surrounding the nucleus is a very small rim of protoplasm. In the denser portions of the connective-tissue framework are bloodvessels of moderate size, with fairly well-formed walls. The rest of the tumor contains small capillaries with distinct walls. Near the inner surface of the sections of the thick portion of the sac are vestiges of smooth muscle fibre, which are only recognizable as bundles in a few places, owing to separation of the individual fibres by the infiltration of the round cells previously described. This area of muscular tissue remaining is quite close to the internal surface of the sac, showing that the mucous membrane and submucosa have sloughed away.

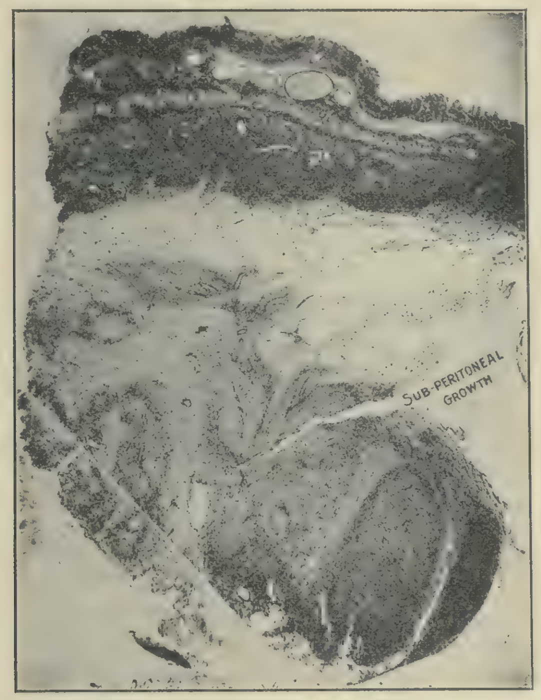
The thin portion of the sac in relation with and adherent to the anterior abdominal wall is covered with peritoneum, and shows itself on section to be composed of two layers—the outer is composed of fibrous tissue, with few nuclei among the connective-tissue bundles; the inner, made up of fibrous tissue infiltrated with chains of the peculiar round cells described. The walls of the bloodvessels here are also well formed. The juncture of these two layers is more or less defined, though in places the infiltration to the fibrous layer is quite evident.

A longitudinal section taken from the posterior wall of the sac, between and including a portion of the afferent and efferent parts of the colon, in connection with the sac, is covered with peritoneum. At each end of this section the bowel is about normal in appearance, excepting for a very slight subperitoneal infiltration of the tumor cells. As we approach the centre of this section, a point corresponding with that portion of the sac between the ends of the bowel, the layers of the intestine become more and more separated, and their appearance altered by the increasing infiltration of the new cells. On the mucous membrane the tubules become shorter and further apart, and, finally, rather abruptly disappear. The muscularis mucosa gradually disappears, but the bloodvessels seem to become more numerous and greatly dilated. In places they have an angiomatous arrangement. The muscular layer, as above mentioned, comes near the surface as the other layers disappear. The individual bundles are greatly infiltrated, so that in the middle of the thickened area only an individual fibre is occasionally seen.

In the region where the sac springs from the colon, and where the tumor infiltration completely surrounds the bowel, the new growth pushes its way between the two layers of the mesentery. Along the cæcum this makes a partial mantle, and on reaching the appendix completely surrounds the entire length of this organ. This surrounding mantle is in places thicker than the intestinal wall itself. The appendix is infiltrated in all its coats, to such an extent in some sections that the normal structure is scarcely to be recognized. In one of these sections an area of degeneration resembling caseous material is to be seen. This is the only area of degeneration found in the tumor.

The lymphatic glands of the mesentery in the region of the tumor are enlarged, of moderate size and consistency, and on section they show a homogeneous structure of whitish color. Microscopically the capsule of the gland and the fibrous trabeculæ show distinct thickening; in places the capsule is distinctly infiltrated with the small round cells, and in some glands there is a mantle of round cells surrounding the gland.

FIG. 2.



Section of bowel wall, with subperitoneal growth.

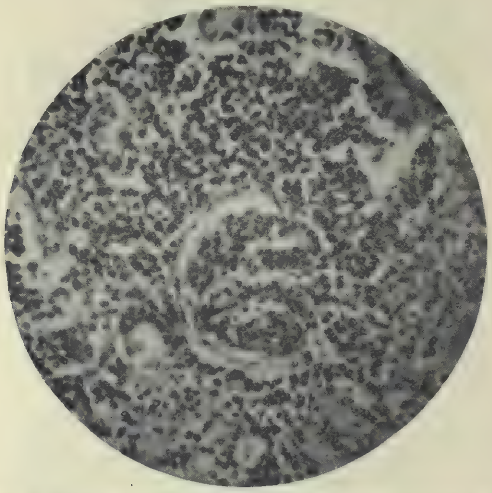
The fatty tissue of the mesentery between the glands shows tracts and heaps of small round cells.

The same structure was observed in the case of the isolated enlarged gland of the mediastinum.

Spleen. The capsule and trabeculæ are distinctly thickened; the Malpighian bodies appear to be slightly enlarged, but they are not distinctly outlined. What was at autopsy thought to be a perisplenititis is found to be a deposit of small round cells similar to those of the tumor.

Kidney. The nodules observed arising from the surface of the kidney are composed of almost pure tumor tissue. They exceptionally show an altered glomerulus, the only remains of the former kidney substance. Between these nodules the kidney structure is more in evidence, although the tubules are separated by the infiltrating tumor cells. The cortex is greatly thickened, this thickening being due to the new growth. The medulla is less involved, and the tubules of the pyramids in many places show only slight changes. The tubules, especially in the cortex, show cloudy swelling, fatty degeneration, necrosis, and in places desquamation of the lining epithelium.

FIG. 3.



Section of kidney, showing glomerulus and infiltrating tumor cells.

Liver. The sections of the liver present a remarkable degree of fatty infiltration and degeneration; in fact, these changes are so pronounced that a normal liver cell can scarcely be seen. Along the interlobular connective tissue, especially surrounding the vessels and ducts, there is a beginning infiltration of the new growth.

Nearly all of the writers on sarcoma of the intestine have prefaced their remarks with comments upon its rarity. Statistical proofs of this are easily found. According to Baltzer,[5] Stort found no cases of sarcoma of the bowel in the records of the Berlin Pathological Institute from 1859 to 1875. Baltzer analyzed fourteen cases, three of his own and the rest collected from the literature. Nothnagel[7] dwells on the comparative infrequency of intestinal sarcoma compared with carcinoma. In the Wiener Allgemeinen Krankenhause, from 1882 to 1893, of 2125 autopsies on cancer cases 243 were of the bowel. Between the same periods, of 243 sarcomata only 3 were of the bowel. He quotes Müller, who found in Berne, of 521 cancers, 41 of the intestine, and of 102 sarcomata but 1 of the intestine, the ileum. Smoler,[6] in fifteen years, from 1883 to 1898, out of 13,036 autopsies found 13 cases of primary sarcoma of the small intestine—a proportion of 1 to 1000. Libman was able to collect about 59 cases in all of sarcoma of the small intestine.

When we compare the relative frequency of sarcoma of the large with that of the small intestine, we find it universally admitted that the latter constitutes the larger class numerically. Disregarding for the present the difference between lymphosarcoma and sarcoma, which, as Nothnagel says, while pathologically distinct, cannot be separated clinically from each other in this locality, we are able to collect the following data: Of 12 cases mentioned by Nothnagel, 1 was duodenal, 3 in the jejunum, 4 in the ileum, 3 in the cæcum, and 1 in the rectum. Nothnagel remarks on the difference between sarcoma and carcinoma of the bowel, the favorite seat of the latter being in the large intestine. This difference is present, he says, at least in the case of lymphosarcoma, to which class 9 of the above tumors belonged. Of Smoler's 13 cases, 2 are included in our list as probably primary in the large intestine, although he includes them in his table of small intestine cases. Treves[13] says that lymphosarcoma is rare in the colon alone, and much more common in the small than in the large intestine. Of 18 cases, in 5 the tumor was located in the stomach, small intestine, and colon; in 1, in the stomach and small intestine; in 3, in the small intestine and colon; in 8, in the small intestine alone, and in only 1 case in the colon alone. He gives the ileocæcal region as a common seat, and states that the tumors grow largest in this locality. Excluding the rectum, he gives the small intestine as the most common site of sarcoma, which, he states, is very rare in the colon. The relative frequency is given by Rosenheim[12] as first in the rectum, and next in the small intestine. Of Blauel's[9] 8 cases of sarcoma of the ileocæcal region we have included 6 in our table as primary in the cæcum. Of 10 cases of sarcoma of the intestine studied by Ablon,[14] 2 were in the large bowel. Libman states that sarcoma by preference occurs in the small intestine, and that in the large intestine (always excepting the rectum) they are much less common, and he quotes Krueger as follows: Of 38 cases, 16 were in the small intestine, 1 in the ileum and cæcum, 2 in the cæcum, 1 in the appendix, 1 in the transverse colon, 1 in the small and large intestine, and 16 in the rectum.

Libman collected 59 cases of sarcoma of the small intestine; we have found in our search but 22 cases of sarcoma of the large intestine. We have analyzed these cases as far as the data we could secure permitted, with the following results:

AGE. The age of the patients ranged from under two years to over sixty. There were seven under ten years; certainly two and probably three between ten and twenty years; four between twenty and thirty; five between thirty and forty; one between forty and fifty; one between fifty and sixty; and one over sixty. The first decade contained the greatest number; the fourth decade the next greatest. There were only three cases past forty years of age.

SEX. The cases were nearly equally divided in point of sex, there being 12 males and 10 females.

LOCATION. Of the 22 cases which we have tabulated as primary sarcomata in the large bowel, in 5 the primary location was open to some doubt, there being, however, a strong probability that it was in the large intestine. In 2 of these there was involvement of the last portion of the ileum. In 1 case—that of Lange—no other part of the intestine was involved, but the growth may have been primary in the ovaries, which were sarcomatous. In 3 other cases, while primary in the large bowel, it involved the ileum by extension. In the remaining 14 cases the large bowel alone was the seat of the sarcoma. When we study the location of these tumors more in detail we find that in 7 cases they were confined to the cæcum (including with it the ileocæcal valve and the appendix); in 5, the cæcum and the ileum were affected; in 3, the cæcum and ascending colon; in 4, the transverse colon; in 1, the descending colon, and in 2, the sigmoid flexure. The cæcum is thus seen to be the most common seat, the next in frequency being the cæcum and ileum; the ileocæcal region comprises the seat of 12 out of 22 cases, or 54.5 per cent. The transverse colon stands next, being the primary seat in 4, or 18.1 per cent.

SIZE. In 8 the size was not stated; in 1 it was said to be the size of a man's head, while in 3 it was the size of a child's head; in 1 it was compared to a cricket-ball. Briefly, the tumors ranged in size from that of a hen's egg to that of a man's head. In one case the growth was in the form of a ring (causing partial obstruction).

VARIETY. In tabulating the tumors from the morphology of the cell we have preserved separate columns for small round-cell sarcoma and lymphosarcoma, although it is difficult to make any definite boundary between these two classes. Where the reporters have described them as such, or from their histological examination they have seemed to us to fall in this group, we have included them as lymphosarcoma; where they have been described as small round-cell sarcoma we have classified them under this head. In 2 cases the type of cell was not stated. Of the remaining 20, 10, or 50 per cent., were round-cell sarcoma; 9, or 45 per cent., were lymphosarcomata, while 1 was of the spindle-cell variety.

METASTASIS. Of 19 cases in which the data as to metastasis was given the abdominal lymphatic glands were involved in 13, or 68.4 per cent.; the peritoneum in 5, or 26.3 per cent.; the small intestine (by metastasis, not by extension) in 2, or 10.5 per cent.; the lung in 2, or

10.5 per cent.; the kidney in 2, or 10.5 per cent.; the spleen in 2, or 10.5 per cent.; the liver in 3, or 15.7 per cent.; other glands in 2, or 10.5 per cent.; the epididymis and spermatic cord in 1; the mesentery (subperitoneally) in 1; the orbit in 1, and in 1 case there was a secondary growth in the large intestine. In 1 case there was no metastasis, and of the 3 cases in which the data was wanting 1 *case recovered after operation.*

The abdominal lymphatics are thus seen to be by far the most common sites for the deposit of metastatic growths, with the peritoneum next in point of frequency. Except where the peritoneum is involved by continuity the road of dissemination of the infecting cells is through the mesentery, and this would explain the frequent and early involvement of these glands which was present in many of the cases at autopsy and in those subjected to radical operation.

ETIOLOGY. The etiology is as obscure as is the case in internal malignant diseases elsewhere. In at least two of our cases there was a strong family predisposition to malignant disease, and there was a history of abdominal traumatism of doubtful influence in two others. Flexner[15] and Libman[8] have called attention to peculiar bodies which they detected in sections from lymphosarcomata of the stomach and small intestine, which they regarded as possibly standing in the relationship of causative organisms.

ORIGIN OF TUMOR. The place of origin of the above tumors is rather difficult to locate on account of the size of the tumor and the involvement of the bowel when the subject presents itself either to the operator or to the pathologist; but from the data of the microscopical examination of the tumors which we have been able to collect, and from the careful examination of our own case, it seems to us that the mucosa or submucosa is the starting-point of these tumors, and, from the normal histology of the intestine, either may be the origin if we take for granted that they have their origin in the lymph follicles. From the mucosa or the submucosa they involve the other coats—the muscular offering the greatest resistance, and, though always infiltrated, traces of this layer are usually found, sometimes as the only remains of the former gut. The subserous coat, from its position, offering very little resistance, we find the greater mass of the tumor usually between the peritoneal covering and the remains of the muscular coat. The serosa itself is rarely perforated. This corresponds with what Baltzer pointed out years ago as the behavior of these tumors in the small intestine. The absence of stenosis and the frequent occurrence of dilatation, sometimes even aneurismal in character, as in our own case, has been explained in the small intestine by the early infiltration and paralysis of the muscular fibres, and the consequent dilatation by accumulation of feces. However, the early involvement of the submucosa, with its plexus of nerves, must not be forgotten as a potent factor in this dilatation.

The *alterations* produced in the segment of bowel involved may be classified as, first, involvement of the whole circumference of the bowel in a rather limited space, forming a rounded tumor with or without dilatation of the lumen. This is the most common condition. The dilatation may be actually aneurismal in extent, due to stretching of the infiltrated wall or to extensive ulceration and breaking down of the interior of the tumor. In about 20 per cent. of these cases the tumor was situated only on one side of the gut. Again, the bowel may be converted into a thick-walled tube, the infiltration extending over a considerable distance in the bowel. In the transverse colon the tumor tends to proliferate in the great omentum, the bowel losing itself in the mass. In only one case was the tumor of the narrow, ring-shaped, stenosing type often seen in carcinoma.

DEGENERATION. The common degeneration of the tumor consists of ulceration of the mucous membrane over the tumor mass, softening within the tumor mass, and subsequently cavity formation. This softening may lead to perforation, with direct communication to the peritoneum, and suppurative peritonitis (in one case purulent peritonitis was found without discoverable perforation), or perforation may follow adhesion between the tumor and loops of the small intestine, as in Blauel's second case (No. 18).

SYMPTOMATOLOGY. In 5 of the 22 cases little or no clinical history was obtained from the sources at our command. Emaciation was mentioned as being present in 11 cases; in 10 it was not mentioned; in 1 case it was not present. It is thus seen to be a frequent symptom, as might be expected from the nature of disease. In our case, as in several others, it was extreme. In the case in which it was not present death was due to septic peritonitis, and not to cachexia and exhaustion, which are common causes of death.

FEVER was present in 9 cases, usually a moderate elevation, especially noted before death. In 1 case, in which there was a secondary infection (probably with the bacillus aërogenes capsulatus and another organism), there was high fever, running up to 104.4° F. for the last four days of life.

ŒDEMA of both lower extremities was present in 1 case, and of the left lower extremity in our own. Pressure upon the iliac veins might, with general weakness and position, be considered as the cause. Ascites was very rarely present.

TUMOR was detected in 16 cases. It was not detected in 2, not noted in the history in 3 (although 2 of these were operated upon), and in 1 no data were obtainable (Hoffmokl, Case No. 21). The presence of a tumor is thus seen to be a most noticeable symptom.

The *locality* in which the tumor was detected during life varied considerably. In 7 it was outlined in the right iliac fossa, in 1 of these cases there being two other tumors in other localities. In 2 it was primarily in the median umbilical region, one of these later shifting to the right iliac fossa, and the other extending over the greater portion of the abdomen. One was in the epigastric region, and four were situated to the left of the median line, one being in the left umbilical region, one in the left hypogastric region, and two in the left hypochondriac and left lumbar regions. The frequent presence of the tumor in the right iliac region corresponds with the frequent ileocæcal location of the growth. In all of the 7 cases in which the tumor was observed to be situated here, the ileocæcal region was found to be the site of the tumor, with one exception, that in which two other tumors were detected during life, in which the transverse colon was the primary site, and in which there were numerous metastatic growths. The next most common location was to the left of the median line. Of the 2 cases observed in the left umbilical and hypogastric regions, 1 was of the transverse colon, and 1 of the sigmoid flexure. Of the 2 in the left hypochondriac and lumbar regions, 1 was a cæcal tumor with intussusception of the ileum and cæcum into the colon, and one was of the sigmoid flexure. The epigastric tumor sprang from the ileocæcal region of the bowel, and here, also, there was intussusception. Of the two in the umbilical region, one—our own case—was of the cæcum and ascending colon, which afterward shifted to the right iliac region, and one was a tumor of the transverse colon. The sarcomata of the cæcal region of the large intestine are thus seen to be usually observed in the corresponding area of the abdominal surface, but may be detected in the median line, or, where there is an intussusception, in the epigastrium or left hypochondrium and left lumbar region. Tumors of the transverse colon usually occupy a median position, sagging downward; tumors of the sigmoid may be looked for to the left of the median line.

In the majority of cases in which the clinical symptoms were given the tumor was described as hard, sometimes of a smooth and sometimes of a nodular feel, rounded or flat, and in two cases there was a sense of fluctuation elicited on palpating it.

Mobility. It was more than twice as often stated to be movable as immovable, and in two cases it is noted that it moved with respiration. The liver was sometimes displaced.

The tumor was frequently found to be tender on palpation.

GASTRO-INTESTINAL SYMPTOMS. These were mentioned in 14 cases or 63.6 per cent. They were mainly pain, anorexia, and vomiting. Pain was present in the majority of cases; in fact, in only one was it stated to be absent. Several other incomplete cases made no reference to it. In 3 it was increased on taking nourishment, and in 1 during urination. It was twice the first symptom noticed, and it was often severe, periodical in some, acute in some, and colicky in others. It was always referred to the abdomen, but not always to the tumor.

In 3 cases it simulated appendicular pain in character and location, and in these cases the tumor was in the ileocæcal region.

Other occasional symptoms were: bloody stools, 3 cases; diarrhœa, 2 cases, and general dyspeptic symptoms were present in 9.

OBSTRUCTION. The absence of obstruction in the large majority of cases is one of the striking characteristics of this form of malignant disease of the large bowel, and is a characteristic which it shares with sarcoma of the small bowel, and which separates it sharply from carcinoma of the same locality. It was certainly absent in 13, or 59 per cent., and it was not noted in the history, and, therefore, probably absent in 6 cases. It was complete in 1 and incomplete in 1, and in 1 the clinical history was not obtainable. In 1 of the 13 cases obstruction was present once during the course of the disease, from twisting of the tumor, as the symptoms disappeared after manipulation; hence obstruction in its truest sense did not exist in this case.

In the case of complete obstruction (Horn) the seat of the tumor was in the descending colon. It was the only case of the spindle-cell type, and the obstruction was due to almost complete stenosis, with impaction of a small fecal mass. In the case of incomplete obstruction, one of Debrunner's (Case No. 4), the tumor was a ring-shaped, round-cell sarcoma of the sigmoid flexure. Thus the only tumors producing obstruction were located in the descending portion of the large bowel.

Obstruction in this class of tumors involving the small intestine has always been due to intussusception, volvulus, or adhesions. In two of our series of cases *intussusception* was found (both tumors of the ileocæcal region), and in neither did it cause obstruction.

DISTENTION. While not a constant symptom this was observed quite frequently, being especially noted in eight cases, often in a marked degree; in one case only was it due to obstruction.

APPENDICITIS SIMULATED. In Libman's paper on sarcoma of the small intestine he reports five cases, in three of which the clinical picture was very similar to that considered diagnostic of appendicitis. He lays much stress on this important clinical observation, and remarks that in attempting to ascertain whether such resemblance had been noticed before he found that the clinical picture was an unknown one. He is not the first, however, to call attention to the fact that sarcoma of the bowel may closely simulate appendicitis. Orth,[4] in 1890, in speaking of the diagnosis of sarcoma of the intestine, dwelt upon the difficulty in separating some cases of typhlitis and perityphlitis from it. Wharton,[16] in 1892, published a paper entitled "Sarcoma of the Cæcum Simulating Appendicitis," and in the case he reported exploration was necessary to differentiate between these conditions (Case No.

11). He personally narrated to us the history of another case, in which the resemblance was as striking (Case No. 12). In one of Blauel's cases, also, is an attack of supposed appendicitis noted as preceding the discovery of the tumor. The fact that the appendix is very often the seat of infiltration in ileocæcal growths may be partly responsible for the symptoms.

There are practically no data in the cases which we have collected in reference to the condition of the blood, although the patients were often said to be anæmic. One case (Fisher, Case No. 19) gives the blood examination three days before death: Hæmoglobin, 50 per cent.; no poikilocytosis or leucocytosis. There is a similar lack of data in the urinary examinations. In our own case albumin was noted late in the course of the disease. In Baracz's case blood cells and blood casts were present in small quantity, without involvement of the kidney. In two cases the urine was normal.

SECONDARY INFECTION. In Fisher's case, where the sarcoma was located in the cæcum, the patient, a male, aged twenty-eight years, first detected the tumor three weeks before admission to the hospital. One week later he developed abdominal pain, followed by swelling of the gums and bleeding, and later by the appearance of a purpuric rash liberally scattered over the front of the body and the neck and arms. Epistaxis was present. The blood showed 50 per cent. hæmoglobin, and no leucocytes or poikilocytes. There was irregular fever during the three days he was under observation in the hospital. He died, and at the autopsy the subcutaneous tissues, especially of the neck and scrotum, and the peritoneal cavity, were distended with gas; and there were small gaseous cysts scattered thickly through the tumor and the spleen, and present in the liver, and to a less extent in the kidney. Aërobic cultures were sterile; anaërobic not made. Microscopically many bacilli were found in the growth among the sarcoma cells around the cysts, often in pairs, and showing a clear space—probably an unstained capsule—around each bacillus. He regarded this germ as probably the bacillus aërogenes capsulatus, and the infection was probably a mixed one. He refers to the case of Hilton Fagge as showing the association of sarcoma with purpura. He thinks the sarcoma acts by lowering resistance and, at the same time, providing a portal of entrance for the germ. Hilton Fagge's[17] case was one of sarcoma of the end of the ileum and the ileocæcal valve, and the symptoms bore a striking resemblance in some points to those of Fisher's case just described. It is not included in our list of cases. The symptoms were entirely those of secondary infection. After some exposure the patient suffered for several weeks from scattered pains in some of the joints, especially the hips and shoulders, without effusion, and had fever and acid sweats. When admitted to the hospital about a month later he was supposed to have rheumatic fever. He then developed a purpuric rash, with hæmaturia, great swelling of the eyelids and scrotum, and ecchymosis of the conjunctivæ. Nodules appeared at the sites of some of the purpuric spots. After death, about two months after the onset of the symptoms, decomposition rapidly set in, and sixteen hours later, at the time of an autopsy, was quite advanced. The scrotum, thighs, and upper arms were emphysematous. The nodules in the skin proved to be sarcomatous.

DURATION. It is difficult to estimate the duration of the disease in this class of cases, as in all of internal malignant disease where the history and the symptomatology have to be depended upon, for the new growth is undoubtedly present for some time before the patient or the physician discovers it. Hence the duration can be estimated only from the time of onset of the symptoms. In the cases not subjected to radical operation, the duration of life varied from one to eighteen months; in the cases in which a radical operation was performed, the duration of symptoms varied from one week to five years before operation, although in the latter case the tumor had been observed for only eight months. One case not operated upon gave no definite symptoms until obstruction developed a few days before death.

The usual causes of death in non-operative cases were cachexia and exhaustion. These were noted in at least six cases—in one, associated with recurrence after the operation. In another case with wide-spread metastasis the cause of death was given as heart failure; this was also probably due to exhaustion. Two cases died of purulent peritonitis, probably due to infection from the bowel; in one of these cases there was incomplete obstruction. One case died of acute obstruction, and another from mixed infection (purpura hemorrhagica).

Fourteen of the 22 cases were subjected to operation. In 4 cases the scope of the operation was purely exploratory, no attempt at removal being carried out. In 10 cases resection of the bowel was performed; 5 recovered from the operation, and 5 died as a result of it—a mortality and recovery rate of 50 per cent. each. Of the 5 cases that recovered 1 died of recurrence after forty-seven days. In 1 no data, beyond the fact of recovery, were attainable; 1 was well after six months; 1 after seven months; 1 after three years. The last case (Orth's) had been operated on five years previously for sarcoma of the ovaries; while the growth in the bowel may have been secondary to that in the pelvis, extirpated five years before, it is included here because of the length of time intervening, and because no other portion of the bowel was affected. In at least 4 of the 5 successful cases enlarged lymphatics were removed from the mesentery; and the fact that these cases recovered shows that the prognosis need not be bad on this account alone, and also the advisability of searching for and removing them.

DIAGNOSIS. The diagnosis of intestinal sarcoma, as of all intra-abdominal tumors, is a matter of much uncertainty. As Osler says, it is here that Bishop Butler's maxim that "probability is the rule of life" finds true application. Of 14 of our cases in which we have recorded the diagnosis made before operation or autopsy, in only 2 can the tumors be said to have been fairly accurately localized; in Bouilly's case a diagnosis of malignant tumor of the intestine having been made, and in Orth's, one of mesenteric tumor. They were taken for tumors of the kidney, the omentum, the ovary, the peritoneum, the lymphatic glands, and in two cases they strongly simulated appendicitis—an observation of considerable importance. Again, the presence of metastasis to the lymph glands and the peritoneum may give rise to the presence of multiple tumors, which may be very confusing. We will briefly summarize the prominent symptoms presented in our cases, and then compare them with those offered by sarcoma of the small bowel and by carcinoma of the intestine.

The primary symptoms are gastro-intestinal manifestations of a dyspeptic type, especially abdominal pain, anorexia, and vomiting; progressive, rapid emaciation; moderate fever; abdominal distention, usually without ascites, but occasionally associated with œdema of the lower extremities; and the presence of a tumor, which is more often movable than immovable, frequently tender, usually of firm consistence, and often located in the right iliac region. The absence of obstruction in the great majority of cases is of great significance. The above chain of symptoms occur in persons of any age, but with greatest frequency in those under forty years, and with relative frequency in the early years of life. The group of symptoms cited does not differ materially from that associated with sarcoma of the small intestine, except, perhaps, the more frequent location of the tumor in the right iliac fossa in disease of the large intestine, owing to the frequent location in the cæcal region. The tumor may be very tender in the case of the large intestine, in which it probably does not differ from some cases of tumor of the small bowel, which in the majority of instances, however, are said to be slightly or not at all tender. Both are liable to be complicated by intussusception. König[18] believes invagination in intestinal tumors to be more common than is usually supposed, citing two cases in discussion.

Libman's statistics show that in the small intestine sarcoma may be found at all ages, although a large percentage of his cases were past thirty. A peculiar paleness or lividity of the complexion has also been described as rather characteristic of cases of sarcoma of the small intestine by both Baltzer and Libman. The differential diagnosis between this tumor of the intestine and carcinoma of the bowel, as well as between it and other intra-abdominal tumors, will, of course, arise. The first question is the only one we need refer to here. Baltzer laid stress on the age, sarcoma occurring earlier; the more rapid growth of sarcoma; the absence of obstruction, of marked tenderness, and of pain during defecation; the early appearance of cachexia and the much greater prominence of general over local symptoms. Libman believes carcinoma of the bowel to be more common than Baltzer supposes in early life, but grants that under fifteen years the chances are in favor of sarcoma; he dwells on the absence of external glandular involvement, the absence of tenderness, and the large size of the growth in cases of sarcoma.

The main points of differentiation would seem to be in a sarcoma of the large bowel, its appearance in the majority of cases in early life (under forty), the early appearance, rapid growth, and large size of the tumor, the quick cachexia, and the absence of obstruction in most of the cases. Pain and tenderness may be present in both; but pain is an early and rather constant symptom in sarcoma of the large intestine, while in carcinoma it does not usually manifest itself until symptoms of obstruction develop.

PROGNOSIS AND TREATMENT. The prognosis without operation is, of course, bad. The life of the patient may be prolonged through a longer or shorter period of suffering, but medicinal treatment of specific nature remains to be discovered. Libman urges the use of arsenic where resection cannot be practised, calling attention to the fact that genuine cases of lymphosarcoma, usually multiple, or of the skin, have been cured by its exhibition, either internally or by injection. We know of no cases of intestinal sarcoma so relieved. The same is true of the use of Coley's fluid. On the other hand, operation, with resection of the growth, offers a fair chance for recovery in cases taken sufficiently early, the prognosis being at least as good, once the tumor can be safely removed, as in sarcoma elsewhere. It is contraindicated in cases far advanced in cachexia, which would be unable to stand the shock of operation, or where there is any other reason to believe that the widespread metastasis so characteristic of the later stages is present. In cases seen early, and in doubtful cases, exploratory laparotomy should be undertaken; 14 out of our 22 cases were operated upon. In 4 the operation was simply exploratory, no attempt being made to remove the tumor. In 10 cases resection was practised; 5 of these died as a result of the operation, either of shock or of peritonitis. Of the 5 that survived the operation, 1 died in forty-seven days of recurrence. Here, certainly, some metastatic growth had been present and not detected at operation. Of the remaining 4 all were living at the time of reporting. This was six months later in 1 case, seven months later in 1, three years in 1, and not stated in 1. In at least 4 of these 5 cases, as has already been remarked, enlarged mesenteric glands were removed at the operation, showing that the presence of metastasis to the lymphatics is no contraindication to operation, and also the necessity of searching for these glands and removing them, if a radical operation is to be performed.

TABLE OF CASES.

Reporter.	Sex and age.	Variety.	Location.	Duration.	Metastasis.	Operation.	Remarks.
1. H. Arnott, Trans. Path. Soc. London, 1874, xxv.	M. 4 yrs.	Lympho-sarcoma (lymphoma).	Transverse colon.	A little over 2 months.	Mesenteric glands, kidney, liver, epididymis, spermatic cord, skin of abdomen.	None.	Died from purulent peritonitis.
2. W. Horn, Hamburg, 1882, quoted by Orth, loc. cit.	F. youth.	Spindle-cell sarcoma.	Descending colon; stenosis of gut.	Unknown; no symptoms before obstruction developed.	Not stated.	None.	Death from acute intestinal obstruction due to stenosis of intestine.
3. A. Debrunner, Inaug. Dissert., Zurich, 1883, quoted by Orth	M. 5 yrs.	Round-cell sarcoma.	Transverse colon.	About 7 weeks.	To omentum, whole abdominal cavity seem'd filled with white or pale red tumors.	None.	Death from exhaustion.
4. A. Debrunner, loc. cit.	F. 16 yrs.	Round-cell sarcoma.	Sigmoid flexure, Some stenosis.	4 months.	Retroperiton'l glands, left ovary, apex of left lung.	None.	Death from peritonitis.
5. H. Beck, Zeitschr f. Heilkunde, 1884, v. p. 442.	F. 59 yrs.	Lympho-sarcoma.	Cæcum and ileum.	Not stated.	Cervical lymph gl'nds, both lungs, encroaching on pleura and pericardium, spleen, stomach, ileum, and mesenteric glands.	None.	Diagnosed lymphoma of cervical and abdominal lymphatic glands; death from heart failure.
6. F. Lange, New York Med. Journ., 1886, xliii. p. 199.	F. 32 yrs.	Not stated.	Transverse colon.	Uncertain.	Omentum, mesenteric glands, both ovaries.	Resection of bowel, removal of ovarian tumors.	Primary seat doubtful; possibly in ovary. Death from septic peritonitis on ninth day; leakage probably from incessant vomiting.
7. Bouilly, Bull. et Mém. de la Soc. de Chir. de Paris, 1888, n. s., xiv. p. 601.	F. 44 yrs.	Lympho-sarcoma.	Cæcum and ileum.	Symptoms for 5 years; tumor for 8 months.	Lymphatic glands in mesentery.	Resection.	Recovered; well seven months later.
8. L. Orth, Inaug. Dissert., Heidelberg, 1890. "Ueber die Sarkome des Darms, Mesenteriums u. Retro-peritonealen Raums."	F. 34 yrs.	Lympho-sarcoma (alveolar)	Transverse colon.	3 months.	Lymphatic glands of mesentery.	Resection (Czerny).	Had ovaries removed for sarcoma five years before; living and well three years later.
9. R. v. Baracz, Arch. f. klin. Chirurg., 1891, xlii. p. 501.	M. 8 yrs.	Round-cell sarcoma.	Cæcum; tumor formed apex of ileo cæcal intussusception.	13 weeks.	A nodule in neighborh'd of ileo-cæcal valve.	Lumbar incision; resection of tumor and intussusception.	Diagnosis: malignant growth in a movable left kidney or in descending colon. Death from shock second day.
10. E. Becker, Deutsche Zeit. f. Chirurgie, 1894, xxxix.	M. 35 yrs.	Round-cell. sarcoma.	Cæcum.	5 weeks before operation; lived 47 dys. after operation.	Not stated.	Resection.	Recovery from operation; death from recurrence.

Reporter.	Sex and age.	Variety.	Location.	Duration.	Metastasis.	Operation.	Remarks.
11. H. R. Wharton, International Clinics, 1894, 4th series ii. p. 199.	F. under 2 yrs.	Round-cell.	Cæcum.	Sick several weeks before admission; still alive several months later.	To orbit.	Exploratory; portion removed for examination.	Symptoms simulated appendicitis before operation; when reported tumor was growing and orbital sarcoma had developed.
12. H. R. Wharton, personal communication.	M. 21 yrs.	Round. cell.	Cæcum.	About two months.	To peritoneum.	Exploratory.	Resembled acute appendicitis at onset; died of cachexia about six weeks after operation.
13. R. Abbe, Annals of Surgery, 1895, xxi. p. 592.	M. 6 yrs.	Not stated; no microscopical examinat'n	Cæcum and ascending colon.	Symptoms for 1 week.	Mesenteric glands.	Resection.	Death from shock 36 hrs. after operation.
14. C. Levi, Bull. de la Soc. Anat. d. Paris, 1895, lxx. p. 68.	F. 38 yrs.	Round-cell.	Sigmoid flexure.	2 months.	None.	Excision (Tuffier); formation of artificial anus; true nature not diag. until removed.	Death 2 days after operation; fatty liver, weighing 3200 grammes.
15. F. Smoler, Prager Med. Woch., 1898, xxiii. p. 145.	M. 27 yrs.	Lymphosarcoma.	Cæcum, ileum, and ascending colon.	Not stated.	Mesenteric glands.	Resection.	Death 2 days after operation, from septic peritonitis.
16. F. Smoler, loc. cit.	M. 19 yrs.	Lymphosarcoma.	Cæcum and ileum.	Not stated.	Peritoneum.	None.	
17. Blauel, Virch. Archiv, 1900, clxii. p. 487.	M. 33 yrs.	Round-cell.	Cæcum and ascending colon.	18 months.	Retroperitoneal and portal lymph glands.	Tum. punctured, later incised and drained; opening communicated thro' tum. cavity with bowel	Colon bacillus found in fluid evacuated. Death from exhaustion 4 days after opening.
18. Blauel, loc. cit.	F. 66 yrs.	Round-cell.	Cæcum.	7 months.	Mesenteric and retroperitoneal glands and liver.	Exploratory.	Died 25 days after operation; anastomosis between tumor cavity and two loops of small intestine resembled tuberculous condit'n.
19. T. Fisher, Bristol Med.-Chir. Journ., 1901, p. 29.	M. 28 yrs.	Lymphosarcoma.	Cæcum and ileum.	3½ weeks.	Few small subperitoneal growths in mesentery.	None.	Purpura hemorrhagica; infection by bacillus probably B. aërogenes capsulatus.
20. C. Van Zwalenberg, Journ. Amer. Med. Assoc., March 9, 1901.	M. 5 yrs.	Lymphosarcoma.	Cæcum; partial intussusception of ileum and vermiform into cæcum	5 months.	Mesenteric glands and ileum.	Resection.	Recov.; 6 mo. later was well; mother and paternal grandmother died of sarcoma.
21. Hofmokl, quoted by Van Zwalenberg.	F. 24 yrs.	Lymphosarcoma (adeno-(sarcoma)	Cæcum.	Not stated.	Not stated.	Resection.	Recovery.
22. Jopson and White.	M. 4 yrs.	Round-cell.	Cæcum and ascending colon.	Probably nine or ten months.	Mesenteric glands, peritoneum, kidney, spleen, and liver.	None.	Liver large and fatty, with some tumor infiltration.

An operation attended with a mortality of 50 per cent. is a formidable one, and not to be lightly recommended; but when we consider the brief duration of life without it—about five and one-half months being the average in the cases not operated upon—and the fairly good results in cases which survive resection, the operation, it would appear, should be advised when thorough removal seems feasible or likely. The section of the bowel should be made through a healthy area, well to each side of the microscopically diseased portion, in order to get beyond the infiltrating cells spreading, sheet-like, in the submucosa and subserosa. When, on opening the peritoneal cavity, the lymphatics and peritoneum are found extensively involved, and the liver and kidneys large on palpation—and, perhaps, nodular—simple closure of the wound will be all that can be done unless obstruction be present, when the formation of an artificial anus above the stenosed area would be indicated.

Van Zwalenberg,[10] in a study of 15 cases of resection of the bowel in various regions for sarcoma, found 9 recoveries and 6 deaths. Children stood operation very well. Of 5 cases under ten years of age only 1 died.

In preparing our list of cases we have excluded those reported by Perceval,[19] W. S. Thorne,[20] and Djemil-Pacha.[21] In Perceval's case the nature of the tumor is too uncertain to classify it; in Thorne's, from the histological examination, the tumor was probably a carcinoma, and in Djemil-Pacha's case, one of sarcoma of the great omentum and transverse colon, the tumor was probably primary in the omentum.

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CARCINOMA OF THE EYELIDS, WITH SECONDARY INVOLVEMENT OF THE EYEBALL; REMOVAL OF THE GROWTH BY EXTENSIVE PLASTIC OPERATIONS; RECURRENCE.

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CLINICAL REPORT BY DR. POSEY.

S. L., female, 61 years old, came to the Howard Hospital April 15, 1896, on account of an ulcerated condition of her right eyelid, which was occasioning her much annoyance and was threatening the loss of the eye. She said that the ulcers had originated in a small mole, which had appeared at about the middle of the lower lid some ten years previously, that the mole had remained quiescent until she picked it, and that after this it had slowly extended, eating away the lid, until it had wrought the damage from which she now sought relief. The ulcerative process had been a painless one, but had been accompanied by severe bleeding when the parts were irritated. Her health was excellent.

Upon admission, the condition of the patient was pitiable, and, so far as the eyes were concerned, desperate. The left eye was absent, inquiry eliciting that it had been removed at the Wills' Eye Hosptal on account of glaucoma; the condition of the right eye also was such that it appeared as though it too would soon be lost, for, as is well shown in Figure I, the lids were almost entirely destroyed and offered but little protection to the eyeball, which already showed the effects of the irritation to which it was exposed in consequence. The upper lid was much affected, the outer third of its ciliary margin being extensively ulcerated, and the corresponding portion of the inner third also showed signs of breaking down. The cornea was still clear and permitted a glaucomatous excavation in the head of the nerve to be seen with the ophthalmoscope. As a result of the ulceration and the adhesions, the globe was fixed and its rotary power much restricted. The upper lid could be elevated but little, owing to the adhesions at both canthi, so that the patient threw her head back when she wanted to see distinctly. Vision equalled 5/12 and with a +S. 4 D. lens, type 0.50 D. was read from 30 to 40 cm.

Extirpation of the growth was at once advised, though the patient was made aware that the loss of the eye was rendered probable, partly upon account of the damage already done to the lower half of the globe by exposure, and partly upon account of the extensive removal of orbital tissue which the radical extirpation of the ulcer would necessitate. The patient's consent was obtained, however, and she was admitted to the hospital, where the writer performed the following operation, with the advice and assistance of Dr. Charles H. Frazier, one of the general surgeons to the hospital.

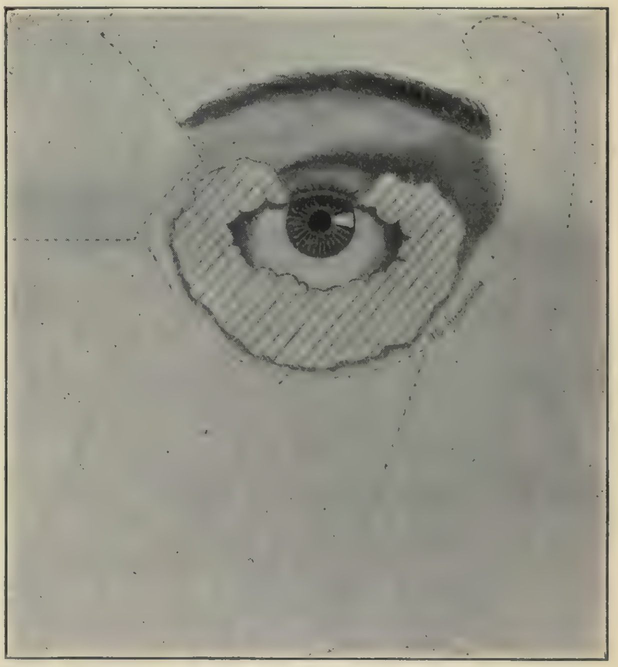

FIG. 1.

An incision was made in the skin the entire length of the lower orbital rim and parallel with it, but far enough below to fall in sound tissue. The ulcerous mass was then grasped firmly with dressing forceps and freed with some difficulty from its attachments, as it was found to have involved the floor of the orbit to a considerable depth, and to have formed very close connections with the sublying tissues. Great care was exercised to avoid wounding the globe, but on account of the extensive dissection required to extirpate the mass, its circulation was greatly interfered with and the bulbar conjunctiva became greatly injected. After the growth in the floor of the orbit had been disposed of, the upper lid was divided by vertical incisions with scissors and the ulcerated tissue at both canthi removed, so that only the central portion of the lid remained. The growth had spread deep into the orbit at the inner canthus, and it was with great difficulty that it was removed from that position on account of profuse hemorrhage. The excision of the ulcerated areas being accomplished, it now became a question as to how the large areas both in the region of the lower and upper lids, which had been denuded by the operation, should be filled in. It was obvious that any attempt to restore the cul-de-sacs would be futile, and that the only procedure which was possible, was to cover in the orbit as well as possible by flaps taken from the surrounding parts of the face. As the skin there was well adapted for transplantation, being full and redundant, the writer hoped to have speedy union follow this transplantation and thought that granulations would soon fill up the orbit from below. A large quadrilateral flap was accordingly obtained from the cheek immediately below the incision which had been made parallel with the lower orbital rim, the vertical lines of the incision being carried below the angle of the mouth. To fill in the gap at the outer canthus, another quadrilateral flap was dissected from the temple, while the inner canthus was covered by a flap taken from above the root of the nose. The lower and the temporal flaps were carefully undermined from the sublying tissues and slid forward into the new position they were to occupy. The flap for the inner canthus, however, was cut free from the surrounding skin and twisted down into position. The three flaps were then stitched together, and to the small portion of the upper lid which still remained, in such a manner that the eye and the orbit were perfectly covered and without tension. (Figure 2.) Better to approximate the wound, and to make firm pressure on the field of operation, and thereby prevent any tendency to bogginess under the large lower flap, two broad bands of rubber adhesive plaster were passed from the angle of the chin diagonally across the face, and fixed over the left eye, and a firm compress bandage was applied over this. The wound was dressed on the third day, and as there were no signs of tension or suppuration, a lighter dressing was applied. Two days later the adhesive strips were removed, and the union of the flaps found to be almost perfect, except at the inner angle of the orbit, where there was some slight superficial suppuration at the points of insertion of several of the stitches. The temperature was normal after the operation, there was no pain and the patient was in the best of spirits. Three days later the stitches were removed and the globe carefully inspected. The cornea was clear, the globe was quite white, and the patient said she could see as well as before the operation.

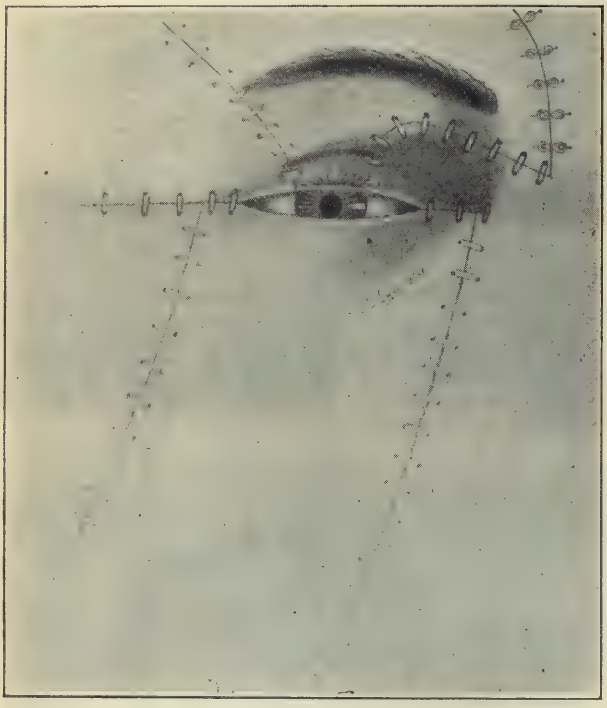

FIG. 2.

The dressings were changed daily by the resident physician, and the wound reported to be doing well. After a lapse of three days, however, signs of panophthalmitis succeeded; the cornea became hazy and necrotic in its entire lower half; bulbar chemosis was intense, and the iris was thickened and discolored. There were no signs of suppuration in the orbit, however, and the temperature was normal. Compresses of hot boracic acid were applied constantly night and day, and the patient given full doses of strychnine and quinine; a weak solution of eserine was also ordered. Under this plan of treatment, the eye gradually become less inflamed, and, at the end of three weeks, was almost quiet. The line of union of the flaps was perfect everywhere, the orbit had filled with granulations, and there was no evidence of any return of the growth. The lower flap had become tightly adherent to the globe below, while the upper lid completely covered the cornea on account of the external and internal adhesions which had been formed. The patient returned to the hospital at intervals of several months after the operation, and at the last visit it was recorded that the palpebral fissure was reduced to a slit about 7 mm. long and 3 mm. broad, and that it was only possible to obtain a view of the lower 2 mm. of the cornea, the rest being hidden by the upper lid. A plastic operation was advised, to free the adhesions and liberate, in a measure, the upper lid. She would not consent to this, and was lost sight of for two years, not returning to the clinic until last Summer, when she reported at the hospital for the relief of intense pain in the eye and temple which she said had been very troublesome for several months previously. Examination now showed considerable swelling of the upper lid and ulceration of the skin which was adherent to the globe below, which appeared to be of an epitheliomatous character. The globe itself was fixed and was in a state of absolute glaucoma, the tension equaling +3.

Admission into the hospital was advised, for the enucleation of the eye and the exenteration of the orbit, if this latter precedure should prove necessary. The patient's consent being obtained, ether was administered and the globe enucleated, and as the floor of the orbit seemed to be completely filled up with the epitheliomatous mass, and the upper lid was also involved externally by it, the contents were completely removed. Recovery was rapid, the orbit filling in rapidly with healthy granulations, and 6 months after the operation, the last time the writer had an opportunity of seeing the patient, there had been no recurrence of the epithelioma.

PATHOLOGICAL REPORT BY DR. SHUMWAY.

The eyeball and lids were placed in Müller's solution for 4 weeks, and then carefully hardened in ascending strengths of alcohol, and divided into two halves in a vertical plane, passing through the optic nerve and the cornea. One half was mounted in glycerine jelly; the other half was embedded in celloidin and cut in sections parallel to the original plane. Macroscopically (Figure 3), the eyelids are seen to be very much thickened; the cornea is likewise thickened, and the eyeball is filled with a mass of clotted blood, which hides all the finer details of structure.

Microscopical examination. The eyelids are thickened to about twice their normal dimensions by the presence of a typical carcinoma of the skin. The masses of infiltrating cells are derived from the lower stratum of cells of the epithelium covering the skin surface of the lid. These cells are proliferating rapidly and are spreading through the lymph spaces of the subcutaneous tissue. There are no whorls of cells nor any horny change in the cells, such as are commonly found in carcinoma arising by proliferation of the superficial cells. The lid margins are ulcerated to a considerable depth, and the bloodvessels in the loose areolar tissue of the eyelid are widely distended with blood, and are surrounded by dense collections of round cells. The bloodvessel walls are moderately thickened. The carcinomatous process extends to the conjunctival surface of the eyelids and secondarily involves the eyeball. The cornea is infiltrated throughout with the epithelial cells, and is covered with a thick fungous mass, composed of the same deeply staining cells (Figure 4). The infiltration extends most deeply into the parenchyma in the lower portion, and, passing backward, both above and below, involves the scleral tisues as far as the insertion of the rectus muscles. The parts of the cornea which are free from the carcinoma cells, show many mononuclear round cells between the lamellæ and numerous newly formed bloodvessels. Descemet's membrane is intact, but its endothelial lining is largely absent. The anterior chamber is shallow and is filled with blood and a finely granular exudate; the angles are obliterated by the attachment of the iris and cornea at the periphery. The bloodvessels of the iris are widely distended with blood, their walls are thickened and the iris stroma is atrophic. The vessels of the ciliary processes are likewise distended, and the entire ciliary bodies are detached and infiltrated with free red bloodcorpuscles; the muscle is atrophic. The choroid is detached from the sclera, its vessels are enormously distended, and the choroidal layers are separated by bloodmasses, which are continuous with the blood that fills out the central cavity of the eyeball. The greater portion of the hemorrhagic extravasation is of long standing, the red cells do not stain brightly with the eosin, and there is much bloodpigment scattered through the mass. A short distance posterior to the ciliary region, below, the sclera is thinned, and at a point shows a rupture of its fibers which are forced outward by the bloodcells. The optic nerve presents a deep excavation of the papilla, the lamina cribrosa being forced well back of the normal position. The excavation is partly filled with a finely fibrillar tissue. The retina extends forward as a thin connective tissue membrane, from which all nervous elements have disappeared, for a short distance from the nerve entrance, and is then lost in the blood. The optic nerve is reduced one-half in diameter, and a broad space separates the fibers from the dural sheath. The connective tissue septa are greatly thickened, and the nerve fibers are entirely atrophic.

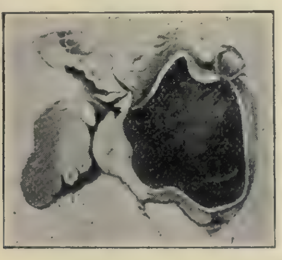

FIG. 3.—Macroscopic appearance of the eyeball and lids. Vitreous full of blood. Eyelids thickened by the infiltrating carcinoma cells.

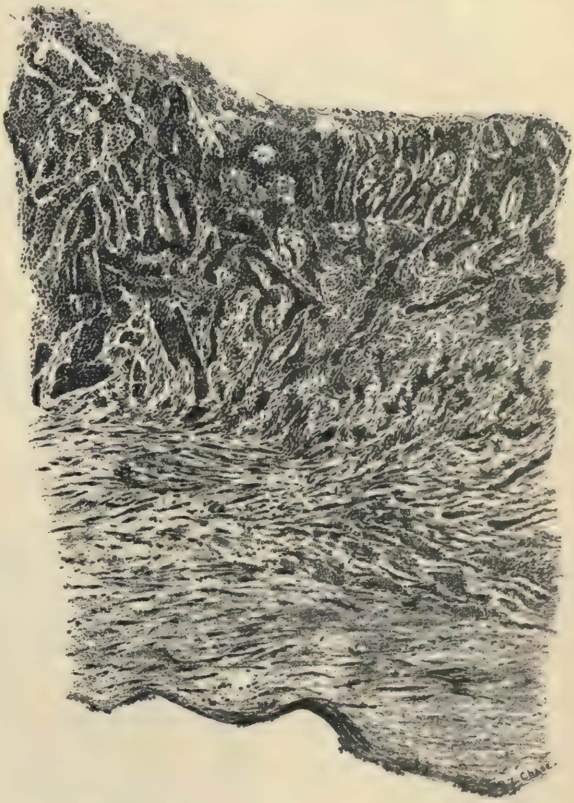

FIG. 4.—Section of growth on cornea.

Diagnosis. Carcinoma of the eyelids, with secondary involvement of the eyeball Absolute glaucoma, rupture of the sclera; extensive intra-ocular hemorrhage. Atrophy of the retina and optic nerve.

PAPILLOMA OF THE CARUNCLE, WITH REPORT OF A CASE.*

By William Campbell Posey, M. D., and Edward A. Shumway, M. D., Philadelphia.

(From the Eye Department of the Howard Hospital, and the Wm. Pepper Laboratory of Clinical Medicine, Phœbe A. Hearst Foundation.)

Papilloma of the conjunctiva is by no means a common growth. In the earlier literature, it was included with a number of other forms under the common name of polyp. Horner,[1] in 1871, was one of the first to give a comprehensive microscopical description of a typical case. Parasotti,[2] in 1884, published two additional cases, and said that they should be separated distinctly from the polyps found on other mucous membranes. Elschnig,[3] in 1889, however, considered the subject more exhaustively, and, following Billroth's classification and Eppinger's researches on similar tumors of the larynx, was enabled to make a satisfactory classification of the polypoid growths on an anatomical basis. This paper was followed by a brilliant set of articles upon the same subject by S. Fuchs,[4] Schirmer,[5] Wagenmann,[6] Zimmermann,[7] Grünert,[8] and La Grange and Mazet,[9] the last two papers containing the complete literature.

In the light of modern pathology, growths which are in the anatomical sense truly polyps, *i. e.*, hyperplastic growths of circumscribed portions of the mucous membrane, including all of its elements, do not occur, or at least have never been reported as growing from the conjunctiva; further, it is to be noted that tumors of the conjunctiva which have the outward appearance of polyps may prove, when subjected to microscopical examination, to be either hard or soft fibroma, adenoma, papilloma or sarcoma. In most of the text-books on ophthalmology, the tumors of the caruncle are not considered of sufficient importance to be mentioned under a separate heading, but are included with those of the conjunctiva, and the subject dismissed with the short remark that papilloma of the conjunctiva may grow also from the caruncle. The number of reported cases of papilloma of the caruncle in which a microscopical examination was made, have, however, been very few, a rather careful examination of the literature discovering only the five following:

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* Read before the Section on Ophthalmology of the College of Physicians of Philadelphia, November 20, 1900.

(1 and 2) Testelin.[10] Two cases, in both of which the growths were situated on the caruncle. These were provided with pedicles, which divided into ten to twelve branches, forming papillæ, the structure of which resembled conjunctival papillæ. He designated them as polyps, but said that the name was a poor one, and was destined to disappear. From his description, however, it is evident that he was dealing with true papillomata.

(3) Hirschberg and Birnbacher.[11] Boy, four and a half years old. In this case, a pale red, raspberry-like growth projected from the caruncle, with other similar growths on the conjunctiva of both upper and lower lid, in the fornix and on the bulbar conjunctiva. Histologically, the growth proved to be a circumscribed hyperplasia of the connective tissue, with very marked prominence of the epithelial covering, and was designated by the authors as a fibroma papillare, or papilloma.

(4) Parasotti.[2] In this instance the patient, who was forty years of age, presented a small tumor of the caruncle, the surface of which, when examined through a lens, seemed to be dotted with small

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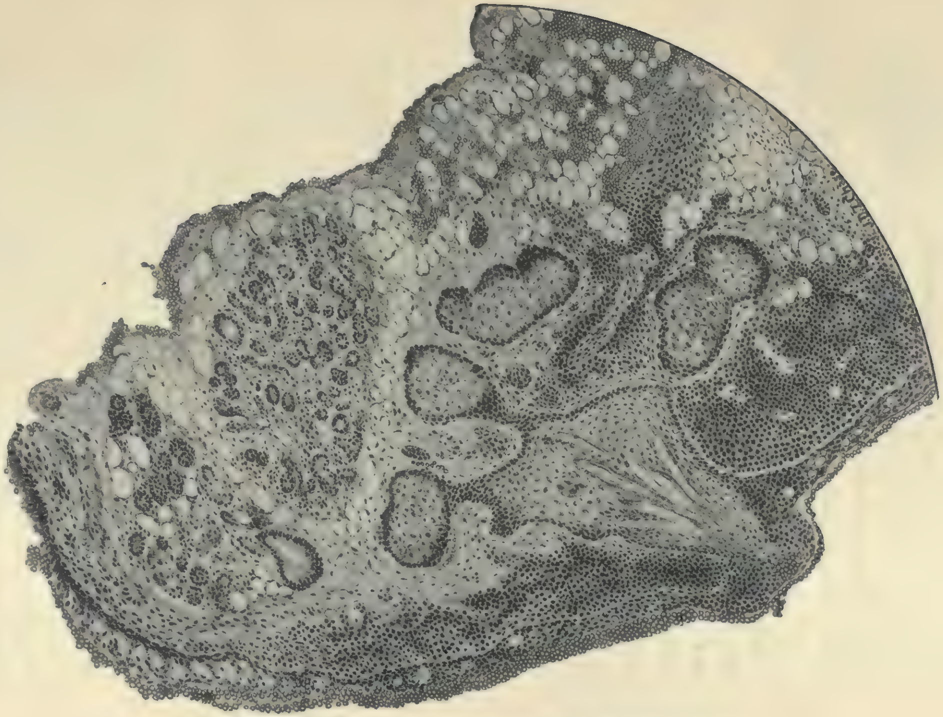

Histological Detail of Caruncle, Showing Round Cell Infiltration.

prominences. Microscopic examination revealed a typical papilloma.

(5) Weeks.[12] The age of the patient is not given, but the growth involved the caruncle and the conjunctiva in the immediate vicinity. It was sessile, about one centimetre in diameter, and recurred twice after careful removal.

To these five cases the following one is added:

H. G., *aet.* sixty years, came to the Howard Hospital one year ago on account of a growth at the inner corner of the right eye. Relief was sought, not because the growth was painful or particularly annoying, but through fear that it might be of a malignant nature.

Examination showed three small growths which were closely clustered at the inner canthus of the right eye. These bodies resembled raspberries in color and consistency, though they were not larger than small mulberries. The larger one was the innermost, and was found to spring from the caruncle by a narrow pedicle, the two smaller growing from the conjunctiva of the lid, close to its ciliary border. The growths were separated from one another by sulci, each tumor being further subdivided by a series of smaller sulci. Their surface was covered with mucus, and showed no tendency to bleed upon handling. The lower lid was somewhat ectropionized.

As the condition of the eyes themselves had no connection with the subject of this paper, it will be sufficient to mention, in passing, that the patient had double cataracts, and that both irides showed curious deviations in their structure

The extirpation of the growth being deemed advisable, the patient was etherized, and the tumor was extirpated by the method of Hasner, as, after due consideration, this seemed the procedure best adapted to repair the loss of tissue in the lids necessitated by the removal of the growth. The restoration of the inner three-fourths of the lower lid was accomplished by taking a flap from the glabella and forehead. The result was most satisfactory, the union of the flaps being by first intention, and the resultant scar astonishingly slight. The danger of recurrence seems also remote, as more than a year has elapsed since the operation, without any evidence of its return being manifest.

The specimens were placed in Müller solution at the time of operation; some of them were subsequently embedded in paraffine and others in celloidin. The sections were stained with hematoxylin-eosin, and by the Van Gieson method. The microscopical examination showed (Fig.) a very marked collection of mononuclear round cells immediately beneath the surface epithelium of the caruncle. The infiltration is a diffuse one, but in two places the cells are grouped in round masses which resemble small lymph nodes. Their form coincides precisely with the ordinary adenoid cells found normally in this position, which have probably been increased as a result of the irritation caused by the presence of the tumor. The epithelium covering the caruncle also shows signs of irritation through the occurrence of numerous goblet cells. As is usual with these cells, they are increased in size, especially in height; the nucleus is located in the deepest part of the cells, and is flattened, while the cell body has assumed a glass-like appearance and has stained light blue with the hematoxylin. In places, the cells form a continuous layer, while in other situations they are isolated.

The main growth arises by a pedicle on the surface of the caruncle. This pedicle is composed of fibrous connective tissue, the fibres of which run parallel to and surround the axial blood-vessels, which are four in number. The covering of the pedicle is composed of several layers of epithelial cells which are continuous with those of the caruncle and contain similar goblet cells. The pedicle then branches, and as these branches proceed from the central stalk, the axial connective tissue becomes less in quantity and assumes a more embryonal type, the fibrils being less closely arranged. They contain in their meshes numerous spindle cells, with long fine processes and many polymorphonuclear leukocytes. The axial vessels are widely distended and the vessel walls are composed of a single layer of endothelium. Surrounding these branching processes of newly-formed connective tissue, are thick mantles of epithelial cells which attain in places a thickness of twenty-five cells. The innermost cells are cylindrical, and the more external are polygonal. The shape of the cells, however, has been much altered by the pressure of the contiguous cells, and, as a consequence, many irregularities of forms are assumed; near the surface they are flattened, and the nuclei stain less well, although there is no horny layer nor evidences of beginning keratosis, such as is commonly found on similar tumors arising from the surface of the skin. In the masses of cells are many goblet forms, or perhaps, to speak more accurately, cells which have undergone mucoid degeneration. These are not confined to the surface layer, but can be found scattered throughout the growth even in the deepest layers. In many places on the surface of the papilla there is, in addition, an infiltration with polymorphonuclear leukocytes. The growths arising from the palpebral conjunctiva have exactly the same structure, consisting of axes of loose connective tissue, branching from a central pedicle, which are closely invested by thick mantles of epithelial cells. There is in no place any infiltration of the subconjunctival tissue with epithelial cells, and the tumor is to be classified as papilloma, or, according to Virchow's designation, fibroma papillare.

The case closely resembles that of Hirschberg and Birnbacher', which has been previously referred to. Clinically, these tumors are rarely malignant in the sense of infiltrating and destroying surrounding tissues; nor do they give metastasis, though they have a marked tendency to recur unless thoroughly removed. As, however, several other forms of tumors, both malignant and benign, though anatomically quite distinct, resemble the papillomata in their clinical appearance, their complete excision with cauterization of the base should always be advised, as a positive diagnosis can only be made by the microscope.

Since the completion of the paper, a further case has been published by O. Kopetzky v. Rechtperg in *Graefe's Archiv. f. Ophthalmologie*, LI, 1, p. 115. "Beitrag zur Kenntnis der papillomatösen Geschwülste der Bindehaut."

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22

THE SURGICAL TREATMENT OF STERILITY DUE TO OBSTRUCTION AT THE EPIDIDYMIS. TOGETHER WITH A STUDY OF THE MORPHOLOGY OF HUMAN SPERMATOZOA.

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It is generally conceded that, as a rule, a barren marriage is dependent upon some abnormal condition of the ovum or of the reproductive organs of the woman. This rule is regarded as one subject to so few exceptions, that, provided the man be suffering from no gross organic lesion or functional derangement, he is rarely subject to examination until years of trial have proved the futility of treating his wife. Of 192 cases of examination of both husband and wife for cause of sterility, collected by Gross, the husband was certainly at fault in 33, or over 17 per cent., 31 presenting azoöspermia, and 2 aspermia.

Absence of spermatozoa from the seminal ejaculations is a positive proof of sterility; the presence of moving spermatozoa in these ejaculations is usually considered an equally positive proof of procreative power, but this belief is based on insufficient evidence. Indeed, there is abundant clinical proof to the effect that systemic conditions which have no appreciable effect upon the motility or conformation of the spermatozoa materially interfere with reproductive power.

It was in the hope that microscopical examination of presumably normal semen might show a structure, conformation, or reaction to stains which would be helpful in distinguishing normal from abnormal spermatozoa that some researches were conducted in the Philadelphia Chemical Laboratory.

The spermatozoön of the higher mammals consists, essentially, of three well-defined parts, viz., the head, the middle piece, and the tail. In each of these parts are finer structures, distinguished only by staining and oil-immersion lenses. What the true character and relationship of this finer anatomy is has been the subject of many investigations.

According to Bardeleben,[3a] who has very carefully examined the human sperm cell, the head is covered by a "cap," which extends backward, and which, in all probability, persists in all higher mammals. (Ballowitz.) The head is composed of an anterior and posterior part, the former staining lightly, the latter showing an avidity for nuclear stains and exhibiting striations ("Valentin'schen querbänder).

In the interior of the head is the internal body ("inneren korper"), described also by Ballowitz and by Miescher, a body which does not stain and which may break up into as many as five pieces. Under very favorable conditions this division has been seen. Bardeleben[3a] states that during the life of the spermatozoön the head changes its form and the contents undergo a rearrangement resulting in the extrusion of part of its substance. Such being the case, the sperm cells are strictly comparable with the egg cells in that this cast-out body corresponds to the polar bodies of the ovum. The small, round corpuscles, so often seen in sperm, are said to be these cast-off "sperm polar bodies." At the present time the general consensus of opinion is against the extrusion of any part of the contents of the sperm cell.

The head of the human spermatozoön, according to Bardeleben,[3a] is provided with a structure by which it penetrates the egg, namely, a "spear" ("spitze"), situated anteriorly and twice as long as the head itself. This spear is extremely attenuated, and, as Bardeleben describes it, is composed of a filamental structure having a protoplasmic covering, and terminating in a triangular tip containing a slightly colored corpuscle. The thread may show several nodal points when stained, and, posteriorly, is joined to the head by an elongated corpuscle. This observation of the "spear" has not been confirmed, so far as we are aware.

Following the head is a neck—very clear, short, and often containing a rounded corpuscle. The middle piece is a continuation of the neck, and varies considerably in length—sometimes longer, sometimes shorter than the head of the same cell. Its finer structure has been made the especial study of Ballowitz,[2d] Benda,[4a] von Brunn, and others. Gibbs[8a b] figures a spiral thread in the middle piece, which observation has been repeatedly confirmed. Benda agrees with von Brunn, that this spiral is formed by the apposition of protoplasmic granules which are not ordinary constituents of protoplasm, but new and probably of some specific function. The spiral is best seen in testicular sperm. (Ballowitz.) Later a cement substance is formed which obscures the thread, but which can, however, be removed by macerating when the thread appears again. The middle piece contains, also, the centrosome, and through it runs the axial filament, a continuation of the centrosome.

This filament is an extremely attenuated thread, which can be traced from the base of the head to the end of the tail. Indeed, the last portion of the tail consists of this axial filament only, and is known as the "Retzius end piece" (Retzius'sche endstück"). Over the tail and middle piece is a protoplasmic covering which can be readily differentiated from the filament by suitable stains. As a tail covering it is very thin, but around the middle piece it may be considerably increased. Bardeleben[3a] says that the quantity of this "protoplasmareste" varies considerably with the age of the cell. He also states that this envelope or "fringe" of protoplasm has a spiral form, giving thereby a rotary motion to the cell as well as the side-to-side movement due to the thrashing of the tail; in other words, the tail is a fin as well as a screw. This observation also lacks confirmation.

Though the various parts of the sperm cell may almost invariably be distinguished, these parts may vary widely in different individuals. The head is found in many sizes and shapes, and anomalous forms have been described by a number of observers. Maddox[14a] describes cells having two heads and one tail; those having two and even three tails, and only one head; he also represents cells which have very large heads. Bardeleben,[3a] too, describes these giant heads, giving their size as 7.5μ long and 3.75μ broad.

TECHNIQUE.

The human sperm cells were examined in their own medium as soon as received, and as much information as possible was gleaned from the fresh preparation. The motility, unless the specimen was too old to exhibit motion, was noted and the kind of cells and corpuscles present with the sperm cells. The material was then diluted with from two to four times its own volume of 0.8 per cent. sodium chloride solution, depending upon the amount of proteid present, and again examined with a high-power lens. So far as could be determined, the solution of sodium chloride had no effect whatever upon the cells. Even when preserved for fifteen days in such a solution (putrefaction being kept down by a few crystals of thymol) the cells showed absolutely no change, so far as could be determined by staining methods. Gibbs found that the heads were more or less affected by salt solution of 0.5 to 5 per cent. strength, some being absolutely dissolved, others remaining quite intact. The work in this research does not confirm the above observation.

If the albuminous substances in the semen were not in very great quantity, a drop of it diluted with salt as above given was placed on a slide, spread out in a thin layer with a cover-glass edge, just as one spreads a blood film, and dried without heat. It was then fixed by placing in an oven and heating to 110° to 120° C., cooling down rather slowly. Slides were fixed, also, by immersing in a mixture of equal parts of absolute alcohol and ether for one-half hour. A very careful comparison was made of cells so prepared with those which were dried in the air, then stained, unfixed, on the slide. So far as could be observed, there was no alteration in the size or shape of the cells.

When an excessive quantity of proteid was present in the material to be examined the above method of diluting with sodium chloride solution did not serve. Examination showed a thin film of proteid over the cells which effectually obscured their finer structure. Therefore, to dissolve this proteid the serum was diluted with about twenty volumes of a 0.12 per cent. sodium carbonate solution in 0.8 per cent. sodium chloride. From this liquid the cells were separated by centrifugalizing for from three to ten minutes, removing them with a pipette, spreading on a slide, drying, and fixing as before.

To determine whether this dilute alkali had any effect upon the cell structure, some actively motile sperm cells were subjected to the treatment as outlined. They were observed at short intervals for about two hours, but not the slightest diminution in their activity could be detected even at the expiration of this period.

A number of staining methods have been tried, among them the following:

The film having been dried and fixed by ether and alcohol, it was stained in a 0.5 per cent. solution of eosin in 70 per cent. alcohol for from five to ten minutes. The excess of stain was washed off with distilled water, and, if the preparation had been overstained, a little 70 per cent. alcohol quickly removed it from the cells. A saturated aqueous solution of methylene blue was then poured on the slide and immediately removed by a jet of pure water. The slide was covered and examined in water to determine the degree to which the stain had penetrated. If the heads were not clearly blue the cover-slip was removed and the methylene blue again applied for a very short time. When a satisfactory preparation had been obtained it was dried in the air and mounted in xylol balsam. A fairly good series of slides can be so obtained.

Ehrlich's Triacid Mixture was used, the method of application being the same as that recommended for staining blood. The difficulty here is that the orange G does not stain the cytoplasm of the sperm cell, hence the various parts lacked definition, though the body and tail were distinctly violet as compared with the blue head.

The method of staining by iron-hæmatoxylin, particularly when supplemented by a cytoplasm stain, has proved, on the whole, the most satisfactory, and possesses the additional advantage of being absolutely permanent, a quality that few anilines can boast. The method consisted of treating the fixed object—and here the fixing agent was heat—with a 2 per cent. solution of iron-alum ($Fe_2(SO_4)_3.K_2SO_4.24H_2O$) for from two to four hours. The excess of iron-alum was then *completely* removed by pure water, and the object treated with a solution of hæmatoxylin (1 per cent. aqueous) for twelve hours or longer. The cells by this time were perfectly black. However, a 1 per cent. solution of iron-alum removed the stain from the cytoplasm, leaving the chromatin of the head, the centrosome, and the axial filament a brilliant blue-black. Care must be taken that the preparation is not over-decolorized. After decolorization a saturated aqueous solution of eosin was added for from one to three minutes. This stained the protoplasmic envelope pink, and, unless the envelope is overstained, the view of the inner structures is not impaired in the least.

An attempt was made to substitute "orange G" for eosin as a cytoplasm stain, using iron-hæmatoxylin as before; but, after staining for twelve hours with a saturated solution of the aniline, the tails and middle pieces showed only the faintest evidences of it. The forepart of the head, however, had absorbed some of the dye. To this preparation was added aqueous eosin for about one minute or even less. The result showed pink tails and middle pieces, black chromatin, and a yellow mass in the anterior part of the head. All these preparations were mounted in balsam.

Magnification. The sperm cells were examined with an optical combination consisting of a Leitz 1/12 homogeneous immersion lens and a No. 1 Bausch & Lomb ocular. The tube length was 170 mm. An Abbe condenser, with double iris diaphragm, served to regulate the light. Such a combination gives a magnification of one thousand diameters.

Measurements. The cells were measured by the aid of a screw micrometer made by Füss, of Berlin. This micrometer scale reads to 1/200 of a millimetre, the divisions being so far apart that one can easily again divide each into four parts, making it possible to read to 1/1600 of a millimetre. The value of the optical combination was determined by the aid of a stage micrometer graduated to 1/100 mm. From a long series of readings it was found that 23.8 divisions on the screw micrometer scale were equivalent to one micron. The observed readings, therefore, were reduced to microns by this factor.

Drawings. The drawings were made with a camera lucida in good daylight, and represent, as nearly as possible, the appearance of the cells. The magnification was determined by projecting the lines of the stage micrometer on the paper and there measuring their distance apart with a 10 centimetre scale graduated to 0.5 of a millimetre, and having a probable error of 0.0005 in 10 centimetres.

MORPHOLOGICAL STUDY.

Specimen of semen marked "Halberstadt." Received December 7, 1901. About thirty-six hours old.

Examination showed no motility. The liquid was opalescent, but there was no marked sediment of mucilaginous material. Bacteria were numerous. Odor not apparent. Cell debris, amyloid corpuscles, etc., very plentiful. The cells could be examined in the undiluted, stained specimen, but better results were obtained by adding an equal volume of physiological salt solution.

Unstained specimens, mixed with salt solution and examined with an oil-immersion lens, showed cells exhibiting a marked variation in size and shape of head. Varied middle pieces could also be seen, particularly those having much of the somatoblast remaining. This appeared as a highly refractive, almost structureless, mass which inclosed the middle piece.

Staining with methylene blue and eosin showed a wide divergence both of form and color, as evidenced in Plate I. This drawing consists of cells selected from one slide. The most common forms are those shown in 2 and 5, where the head is stained entirely or partly blue, the inner body remaining unstained or staining only lightly, and being well defined. The blue stained portion in such heads has only rarely a sharp boundary line, but fades off usually into the lightly stained portion. It frequently, too, sends up tendrils dividing the anterior body, as in Plate IV., cell 5. Such heads may or may not have an abnormal middle piece. Cells having an oblong head, as 1 and 6 in Plate I., and 9 and 10 in Plate III., are also very common in this specimen. In cell 6, Plate I., the chromatin has formed a ring about the cell, sharply defined and bringing out, by contrast, the clear portion above and below.

Cell 5, Plate I., and cell 8, Plate III., show a form not quite so plentiful. The heads here are extremely pointed and generally stain quite dark, without any indication of an inner or anterior body. Cell 5 shows the "acorn form," with an exaggerated point, but cell 8 gave no indication of such a division. That pointed forms exist intermediate between these and such a cell as that shown in Plate III., cell 4, can easily be seen by a glance at those figured in the set of plates.

In addition to such heads one finds them of a much larger type, becoming as enormous, occasionally, as cell 7, in Plate III. It is unusual, however, to find so large a cell having so much of the color-carrying substance. Generally these monster heads have the appearance of cell 3, in Plate IV., and like this, too, are round in form.

Occasionally, in studying this specimen, twin heads were observed, these following the types given in Plates V. and VI., which represent those found in the "Reading" specimen, and will be discussed under that heading.

Cell 1, Plate II., shows two heavy balls (heads ?), one lying above the other, but both inclosed in a protoplasmic envelope. A middle piece and some indication of a centrosome were diligently sought for, but none could be observed. Another anomalous head is figured in Plate IV., cell 2, where we find a very deeply stained ball forming the anterior end of a large sac, chiefly, according to its staining reaction, protoplasmic in character, yet holding some nuclear substance, as shown by the grayish ball in the posterior part. It is possible that this protoplasmic mass represents a much distorted middle piece.

The middle piece in many instances shows a very marked protoplasmic enlargement as well as pronounced exaggerations of form. In cells 1 and 6 of Plate I. we have, apparently, a protoplasmic mass, since the stain is so extremely red, through which the axial thread in the middle piece proper can be distinguished with more or less clearness. Cell 6 shows it very plainly, and as both head and tail are so distinctly blue, the middle piece would, in all probability, correspond were it not for the red protoplasm lying above.

A number of the cells have a protuberance just below the head, as in cell 4, Plate III., containing the centrosome (?). This protuberance may be found at any point along the middle piece, from the head down to the junction of the middle piece and the tail. Cell 3, Plate III., shows it about half-way down the middle piece, while No. 5 shows it only a short distance from the posterior end of the head.

Occasionally, when the staining conditions are very favorable, one can distinguish on the middle piece traces of the spiral thread. It is very difficult to trace, and I have never been able to distinguish more than two turns of the thread.

A very interesting cell is figured in Plate III., cell 9, where the dark, ring-shaped centrosome is clearly seen, and lying in it the long centrosome which has been proved to be the head of the axial filament. Indications of this are seen in many cells, but the clear view has been obtained more frequently in the incompletely developed sperm cell.

The middle pieces of the two-tailed cells show but little structure. In cell 4, Plate II., it seems probable that the axial filament in each tail arises from the two small, dark bodies lying above each filament and at the edge of the middle piece. In cell 2, however, no such bodies could be seen. In this cell one mass extending across the body of the middle piece was seen, and it is quite possible that a higher power or better conditions would resolve it into two bodies.

The tails in these cells showed, here and there, the Retzius end piece, as in Plate I., cell 3, and Plate IV., cell 1. The length of the tail varies much, though it is difficult to be quite sure that some of it has not been broken off. The width of the tail is more striking. From an exceedingly fine filament, as seen in most of the cells, it may widen until it attains such a width as that shown in cell 6, Plate III., or cell 9, where it is also very much wider than usual. These broad tails are never so long as are the finer ones.

Specimen marked "Reading." Received December 13, 1901. Age of specimen, twelve hours.

Liquid was thick, almost opaque, with a heavy, mucilaginous sediment at the bottom. A study of the fresh cells showed a much greater number of giant heads than in "Halberstadt." The motility was very slight.

A second specimen, marked "Reading II.," received December 20th, six hours old, showed a very motile condition of the cells, other conditions remaining the same.

Examination of the fresh material showed a considerable difference in the rates of motion of the various forms of head. This was first noted in the freely moving cells, and later a mucin thread was found which had entangled a large number of cells, holding them, mostly, by their tails, leaving the head and upper part free. These cells struggled violently to get loose, and our observation was that the oblong or pointed heads, having only a small apical body, moved the fastest and succeeded oftenest in freeing themselves from the mucin. When the apical body was large and the cell tended toward the round form, the rate was slower. A number of twin forms were found, but without exception these were quite motionless. The giant heads, too, were non-motile. Certain cells having a marked "protoplasmareste" were very sluggish. One, in particular, in which the protoplasmic mass was quite as large as the head and puffed up like a full balloon, moved very slowly and after the fashion of a measuring-worm. The thrashing and screw motion was quite gone.

These specimens were so full of mucin that the washing with dilute alkali, as elsewhere described, had to be resorted to. Fixing and staining were as described.

A study of these preparations shows at once a marked difference between the size of these cells and those of the "Halberstadt" material. This is brought out in the plates, which are drawn to the same scale as those already discussed. Marked individual variations, also, are easily demonstrable, most of them following the general types of variation seen in the preceding specimen. The twin forms, being fairly abundant, were carefully studied. This variety of sperm cell has been described by Maddox. The two heads and middle pieces may be quite perfect individuals, and be formed either at or just below the end of the middle piece, as in Plate VI., cell 7; or, one middle piece may be sharply marked, as in cell 1. The heads may be mounted on middle pieces of equal length; or, as in cell 5, Plate V., one head may have a very short middle piece. Cell 6 shows one head well developed, the other rudimentary and staining quite a different color. This difference in size is also indicated, but less exaggerated, in cell 7.

In such forms the question of axial filaments naturally arises. Are such cells brought about by actual fusion during spermatogenesis of the hinder portions of the spermatid, or have we two distinct individuals whose tails are bound together by the protoplasmic residue of the testicular cells? Such a question might be partly solved, at least, by the positive demonstration of one or two Retzius' end pieces. A conscientious attempt was made to do this, but without success.

The monster heads in this specimen showed almost exclusively a round form. The chromatin in them was never very marked, being apparently scattered as fine threads over the whole ball. These threads often assume definite, though inconstant shapes, as in cell 9, Plate V., where it has the appearance of a cross, and in cell 2, Plate VI., where it forms a ring around the lower part of the cell. Apical bodies are not visible in these cells. The middle piece of the giant cell is usually represented by a rounded mass pushed close up against the head, showing well-marked chromatin. Long middle pieces are found, however, as seen in cell 9, Plate V., and cell 2, Plate VII. The spiral mark-ing is often seen more readily here than in cells having a normal head. Another prominent feature is two dark bands in the middle piece close to the base of the head, as in cell 1, Plate VI.

Specimens marked "Germantown." The first, received December 16, 1901. About five to six hours old. An opalescent, mucilaginous liquid. Examined fresh, showed *no spermatozoa* and very few cellular elements of any kind. Probably three or four cells would be found in an average field. These consisted chiefly of white blood-corpuscles, with amyloid corpuscles of great variety, and occasionally a cylindrical cell with one eccentric nucleus. In addition, some large pavement epithelium was found. In the fresh material was seen a number of large crystals which refracted light, were shaped like a clam-shell, and had frequently some spicules attached to the hilum of the shell. While the material was fresh no other crystals were observed. When twenty-four hours old many crystals of magnesium ammonium phosphate ($MgNH_4Po_4$) were seen, but the unknown clam-shell crystals had not increased any.

As the cellular elements were so few, and the accurate determination of the presence or absence of spermatozoa so important, the material (about 3 c.c.) was diluted with thirteen times its volume of 0.8 per cent. sodium chloride and centrifuged. The cells were removed from the tube and studied again, but no new features developed, and spermatozoa were not seen. (See Plate VIII.) This examination was made shortly before the operation described elsewhere in this paper.

The second "Germantown" specimen was received January 11, 1902. It was twelve hours old. Examined in the fresh condition it showed the presence of spermatozoa, not so plentiful as usual, but very actively motile. The usual prostatic elements and round testicle cells were also seen.

This material was extremely mucilaginous, hence was washed with dilute alkali and centrifuged. The stained cells are figured in Plate IX. A differential count showed that 50 per cent. of the cells present had either a much enlarged middle piece or one showing a protuberance somewhere along it. In nearly all of them were the middle pieces more marked than is usually observed, this point coming out no matter which method of staining was used. In many cells two protuberances were found, as in cells 8 and 11; and, again, the protoplasmic body, or whatever it may be, seems to be attached very lightly to the cell itself, as in No. 5. No. 7 is a normal cell, showing the round, or collar-like, centrosome and the rod centrosome, from which the axial thread arises, lying in it. This has been noted before, but was seen best and most frequently in these cells.

The usual variety of heads were found, and very occasionally a twin or a two-tailed form.

No. 11 shows a giant head, stained violet, round, and having but little chromatin. The middle piece here is extremely interesting, the large protoplasmic envelope showing clearly, by contrast, the round, dark-blue chromatin mass, which, however, is *not homogeneous*, but seems to be composed of distinct granules. Below this structure, which we believe to be the centrosome, is a distinct blue thread, which runs into and becomes lost in the bullous enlargement forming the base of the middle piece. The axial filament reappears in the tail. Cell 1 shows very excellently the arrangement of centrosomes and axial filament.

Cell 9 has stained a clear blue. This cell corresponds very closely in appearance and size with those found in the testicle itself and figured in Plate X., cells 3 and 4.

Study of Sperm Cells from the Testis and its Appendages. The fresh, human gland was carefully dissected out and an incision made into the rete. A drop of the fluid exuding was placed on a slide with an equal quantity of physiological salt solution, spread out into a thin layer, dried in the air, and fixed as usual. An incision was made, also, into the globus major, cutting across the vasa efferentia. Cells from this portion were prepared as above. Slides were then made from the body of the epididymis, from the junction of the vas with the epididymis, and from the vas deferens itself. All these preparations were stained by iron-hæmatoxylin. Plates X., XI., XII., and XIII. show the type of cells found in the various structures.

In the rete, as shown in Plate X., the cells are often of the giant-headed type, and the heads are uniformly larger than are those which have passed out of the testis. In general, they may be said to lack structure, though occasionally, as in cell 1, Plate X., cross-striations are observed, and certain areas in the head stain less deeply. The large round heads show thin chromatin lines just as do those figured and discussed under the "Reading" specimens.

The middle pieces are long and very clear, save for a dark area which generally occurs at the base of the head, though it may be found further down. It would seem that this dark body corresponds to the centrosome, though it is quite impossible in these preparations to connect it with an axial filament. Generally, too, it lies in a distinct protuberance, as shown in cell 1. At the junction of the tail and middle piece are seen very often two small, round, deeply stained spheres, as in cells 2 and 4. Such spheres have not been observed in any other cells. In cell 3 two such spheres are seen close to the head, and one therefore wonders whether these bodies are not possibly migratory.

The tails are ill-defined and but lightly stained.

These rete cells have been carefully measured, and, as seen from the list of measurements, they are of large size. The type measured corresponds to cells 1, 4, and 5 of Plate X. The cells vary from 3.45μ to 6.75μ in length of head, and from 1.65μ to 3.35μ in width of head. The length of the middle piece is from 6.35μ to 2.75μ. The ratio of width of head to length of head varies considerably—from 1 : 1.3 to 1 : 3.3, the average of ten measurements being a ratio of 1 : 2.15.

The ratio between the length of head and length of middle piece has also been determined for the same ten cells. Here we find the length of middle piece : length of head : : 1 : 0.73 (minimum), and length of middle piece : length of head : : 1 : 1.9 (maximum). The average is 1 : 1.24.

TABLE I.—*Study of Cells from Gland. Rete Testis.*

	Head.		Middle piece.		Tail.		Ratio width of head to length of head	Length of middle piece to length of head
	Length	Width	Length	Width	Length	Width		
1	5.96	2.43	5.0	...	38.94	...	1 : 2.0	1 : 1.19
2	6.34	2.94	5.02	...	44.45	...	1 : 2.1	1 : 1.2
3	3.9	2.85	2.85	...	50.25	...	1 : 1.3	1 : 1.01
4	5.25	3.25	2.75	...	44.55	...	1 : 1.6	1 : 1.9
5	6.25	3.35	5.65	...	...	...	1 : 1.9	1 : 1.10
6	5.55	1.65	6.35	...	51.75	...	1 : 3.3	1 : 0.87
7	7.7	2.35	4.1	...	...	...	1 : 3.2	1 : 1.8
8	6.75	2.85	4.75	...	43.00	...	1 : 2.3	1 : 1.4
9	3.45	2.35	4.7	...	34.80	...	1 : 1.4	1 : 0.73
10	6.50	2.70	4.5	...	40.00	...	1 : 2.4	1 : 1.2
						Aver'ge	1 : 2.15	1 : 1.24

Plate XI. shows cells from the body of the epididymis. Here is seen a great decrease in the size of the head, and it is relatively narrow. Apical bodies are now visible and occasionally are well defined, as in cell 3. The enlargement in the middle piece and its corpuscle are still pronounced, though this structure seems to be more often midway down the middle piece than at its head end. In some cells it is entirely wanting, as in cell 5.

Measurements of these cells show the length of head to be from 3.57μ to 4.78μ. The width of head is from 2.64μ to 3.15μ. The width of the head : the length of the head : : 1 : 1.21 (min.), or 1 : 1.58 (max.). The average is 1 : 1.46.

The ratio between head and middle piece here is length of middle piece : length of head : : 1 : 1.03 (min.), and 1 : 1.83 (max.), an average of 1 : 1.36.

TABLE II.—*Study of Cells from Gland. Body of Epididymis.*

	Head.		Middle piece.		Tail.		Ratio width of head to length of head	Length of middle piece to length of head
	Length	Width	Length	Width	Length	Width		
1	4.20	3.06	2.73	...	30.67	...	1 : 1.37	1 : 1.55
2	4.20	3.02	2.81	...	26.89	...	1 : 1.39	1 : 1.49
3	3.65	2.64	4.49	...	29.83	...	1 : 1.38	1 : 0.81
4	4.78	3.02	2.94	...	27.31	...	1 : 1.58	1 : 1.63
5	3.57	2.94	3.44	...	34.03	...	1 : 1.21	1 : 1.03
6	4.62	2.77	2.52	...	31.09	...	1 : 1.66	1 : 1.83
7	4.49	2.94	3.44	...	26.34	...	1 : 1.52	1 : 1.30
8	4.56	2.89	2.94	...	25.21	...	1 : 1.57	1 : 1.55
9	4.32	2.52	3.36	...	33.61	...	1 : 1.71	1 : 1.28
10	3.86	3.15	3.27	...	28.99	...	1 : 1.22	1 : 1.18
						Aver'ge	1 : 1.46	1 : 1.36

At the junction of the vas deferens with the epididymis the cells correspond still more closely to the normal type, as seen in the upper part of the vas. Plate XII. shows four typical cells, which exhibit but slight differences as compared with the cells of Plate XIII. These cells do, perhaps, show the middle piece more distinctly, and the tail stains more readily. Cell 1 shows distinct evidence of a spiral on the middle piece.

Their measurements are: Length of head from 4.2μ to 5.54μ; width of head, 2.1μ to 3.52μ. The ratio between length and breadth is 1 : 1.04 (min.), and 1 : 1.9 (max.). The average for ten cells is 1 : 1.64. The ratio between length of middle piece and length of head is 1 : 1.2 (min.) and 1 : 2.03 (max.), an average for ten cells of 1 : 1.35.

TABLE III.—*Study of Gland. Junction of Vas and Epididymis.*

	Head.		Middle piece.		Tail.		Ratio width of head to length of head	Length of middle piece to length of head
	Length	Width	Length	Width	Length	Width		
1	4.6	2.45	...	...	50.45	...	1 : 1.8	
2	5.54	3.35	4.11	...	42.85	...	1 : 1.6	1 : 1.34
3	4.74	3.52	2.72	...	...	...	1 : 1.3	1 : 1.7
4	5.12	2.89	2.52	...	32.56	...	1 : 1.7	1 : 2.03
5	4.62	2.56	2.52	...	33.61	...	1 : 1.8	1 : 1.8
6	4.20	2.64	2.94	...	34.45	...	1 : 1.5	1 : 1.4
7	4.95	2.60	4.1	...	33.61	...	1 : 1.9	1 : 1.2
8	4.49	2.43	2.94	...	32.98	...	1 : 1.8	1 : 1.4
9	4.62	2.52	3.06	...	34.87	...	1 : 1.04	1 : 1.5
10	4.32	2.10	3.35	...	35.29	...	1 : 2.05	1 : 1.2
						Aver'ge	1.64	1.35

In the vas deferens we find the usual types of cell, as heretofore described. The cells seem to be perfect in every way, and, when measured, show a length of head varying from 5.12μ to 3.65μ, and a width of 4.1μ to 2.22μ, or a ratio of 1 : 1.1 (min.) to 1 : 1.9 (max.). The average for ten cells in 1 : 1.6.

The ratio between length of middle piece and length of head for these cells is 1 : 0.83 (min.) and 1 : 1.8 (max.), an average of 1 : 1.15.

TABLE IV.—*Study of the Gland. Vas Deferens.*

	Head.		Middle piece.		Tail.		Ratio width of head to length of head	Length of middle piece to length of head
	Length	Width	Length	Width	Length	Width		
1	4.1	...	3.75					
2	5.12	3.44	2.77	...	42.01	...	1 : 1.8	1 : 1.4
3	4.78	4.1	5.63	...	42.05	...	1 : 1.1	1 : 0.84
4	4.62	2.39	4.62	...	42.01	...	1 : 1.9	1 : 1.0
5	4.20	2.60	5.02	...	43.27	...	1 : 1.6	1 : 0.83
6	4.83	2.73	4.83	..	51.05	...	1 : 1.7	1 : 1.0
7	4.62	3.15	3.57	...	43.48	...	1 : 1.4	1 : 1.2
8	4.32	2.22	3.35	...	41.80	...	1 : 1.9	1 : 1.2
9	5.02	2.94	4.20	...	50.42	...	1 : 1.7	1 : 1.1
10	4.20	2.52	3.35	...	42.01	...	1 : 1.6	1 : 1.2
11	3.65	2.72	3.35	...	42.85	...	1 : 1.3	1 : 1.8
						Aver'ge	1 : 1.6	1 : 1.15

A tabulated view of the foregoing ratios is suggestive as indicating the progressive march of the cells.

	Width of head to length of head.	*Length of middle piece to length of head.*
Rete testis	1 : 2.15	1 : 1.24
Body of epididymis	1 : 1.46	1 : 1.36
Junction of vas and epididymis .	1 : 1.64	1 : 1.35
Vas deferens	1 : 1.60	1 : 1.15

GENERAL DISCUSSION. The foregoing statements and illustrations have served to show that the sperm cell of the human subject has a great variety of form and size in each and every part. That it is also prone to exhibit strongly anomalous characters, as twin heads or twin tails, has been emphasized in this study as well as by those observers before quoted. Whether such monstrosities can fertilize the ovum is an unsolved question. If motility is an essential to fertilization the evidence would seem to be negative, since at no time have these forms, or those possessing monster heads, been seen to move.

An explanation of the origin of the different forms of head noted we have been unable to formulate. Such types as the "acorn," the very pointed, long head, the small, round head, etc., cannot be traced so far as development is concerned. On the other hand, the round, clear, lightly staining giant heads are found in the testicle itself, and, so far as could be observed, are the exact counterparts there of the cells which have travelled all the outgoing channels of the tract. With such cells in the rete testis, and forming the great majority of the cells seen, are the large, oblong, homogeneous, but darkly stained heads. The latter are rarely seen outside of the testis; but the giant heads are in about the same proportion, no matter from what part of the tract the spermatozoa are taken.

It seems probable, therefore, that it is the oblong-headed form which, gradually contracting, becomes the common, darkly staining sperm cell. The giant heads may be either cells which have developed to that point, and there had further development arrested, or they may be sports produced by anomalous conditions in the development of the spermatid. That they can hardly be accepted as degenerated forms produced by retrogressive changes in the cell after leaving the testis, during its journey through the various ducts, is settled, probably, by finding them among the cells of the rete testis. Whether they are or are not degenerated forms in spermatogenesis remains to be seen.

The developmental condition of the cell head may, if Watasé's theory holds good, be judged from the result of double staining with a nuclear and a cytoplasm dye. Auerbach has made such a study for egg and sperm cells, and as a result of it states that the sperm head is a *cyanophil* and the egg cell an *eosinophil*, the former staining blue, the latter staining red. He traces, in this way, the chemical changes of spermatogenesis from the primal red staining cell to the blue sperm head, and indicates the progress by the color which the cells absorb. Watasé carries the same principles into the study of the sperm cell itself, and states that some of these heads are quite blue, and therefore fully mature cells; that others are red, and therefore comparable, really, with an egg rather than a sperm cell; and that others still are of a violet color, verging toward either the red or the blue, according to the condition of the cell, whether it be leaning toward the egg or the sperm composition.

Looking at the drawings of cells stained with eosin and methylene blue—Plates I., V., and part of IX.—one is struck at once with the difference in their appearance. The "Halberstadt" specimen shows a clear blue or bright red, while the "Reading" cells show a violet, more or less red in character. Every attempt made to stain a slide of this material so that the color definition would appear as in Plate I. proved a failure. The only clear blue cell ever seen was the one giant head reproduced in

EXPLANATION OF PLATES.

PLATE I.

Eosin. Methylene blue. × 1300 diameters.
Blue heads = perfect cells.
Red heads = immature cells.

PLATE II.

1. Double-headed form.
2, 4, 5. Double-tailed form.
3, 7. Enlargement of middle piece.
6. Normal form.

PLATE III.

1, 2. Normal.
3, 4, 5, 7. Enlargement of middle piece.
7. Giant head.
9, 6. Wide tails.
9. Ring on middle piece.
10. Interior body.
8. Pointed head and somatoblast.

PLATE IV.

Iron. Hæmatoxylin. Eosin. Orange G. × 1300 diameters.
1, 5. Normal.
2. Abnormal form.
4, 6. Slight enlargement of middle piece.
3, 7. Giant heads.

Shows yellow-stained protoplasm in head; pink-stained protoplasm in middle piece and tail.

PLATE V.

Eosin. Methylene blue. × 1300 diameters.
1, 9. Giant heads.
5, 6, 7. Twin heads.
4, 8. Enlargement in middle piece.
2, 3. Normal cells.

Shows violet-stained heads, indicating, according to Watasé, immaturity.

PLATE VI.

3, 4, 6. Normal cells.
5. Acorn head.
2. Giant head.
7. Twin head, showing division below the middle piece.
1. Twin head, showing rudimentary middle piece.

PLATE VII.

Iron. Hæmatoxylin. Eosin. × 1300 diameters.

1. Normal, showing Retzius' end piece and sphere at end of middle piece.

2. Giant head, showing protoplasmic envelope and long middle piece.

3. Distorted head, without visible middle piece.

4. Protoplasmic envelope on head and large somatoblast.

PLATE VIII.

Cellular elements in case of azoöspermatism.

PLATE IX.

× 1200 diameters.

1. Eosin. Iron. Hæmatoxylin. Enlarged middle piece, showing both centrosomes and axial filament.

5. Iron. Hæmatoxylin. Cross-band on head, long middle piece, with protoplasmic corpuscle.

6. Iron. Hæmatoxylin. Shows two centrosomes in middle piece; diffuse chromatin in head.

7. Iron. Hæmatoxylin. Normal form, shows two centrosomes.

8. Iron. Hæmatoxylin. Dense chromatin in head, thick middle piece, with two distinct spheres. This type forms about 50 per cent. of the total number of cells

2. Enlarged middle piece; deep violet head.
3. Clear blue head; corpuscle at end of middle piece.
4. Violet head.
9. Clear blue head. A testicle cell not developed
10. Deep violet head; large middle piece.
11. Giant head; corresponds to those seen in testicle.

PLATE X.

Rete testis, showing cells that correspond to giant forms. Centrosome close to head. All heads much larger than developed forms. 2, 4, show darkly-stained spheres at junction of tails with middle pieces.

PLATE XI.

From body of epididymis. Cells show protuberance in middle piece; prominent centrosomes; diminution in size of head. Tails faint.

PLATE XII.

From junction of vas and epididymis. Shows relative broadening of head, with occasional protuberance of middle piece.

In 4 apical body very marked.

In 1 evidences of spiral middle piece.

PLATE XIII.

From vas deferens. Normal cells showing common forms.

PLATE XIV.

Anastomosis between the vas and the epididymis; sutures passed and the first twisted.

A. Cut surface of epididymis.
B. Lumen of vas.
C. Vas.
D. Epididymis.
E. Vaginal tunic.
F. Cord.

PLATE XV.

Anastomosis between the vas and epididymis; anastomosis accomplished by securing the remaining sutures.

C. Vas.
D. Epididymis.
E. Vaginal tunic.
F. Cord.

PLATE A.

Fresh unstained cells. × 1000 diameters.
About one-half of tail is visible.

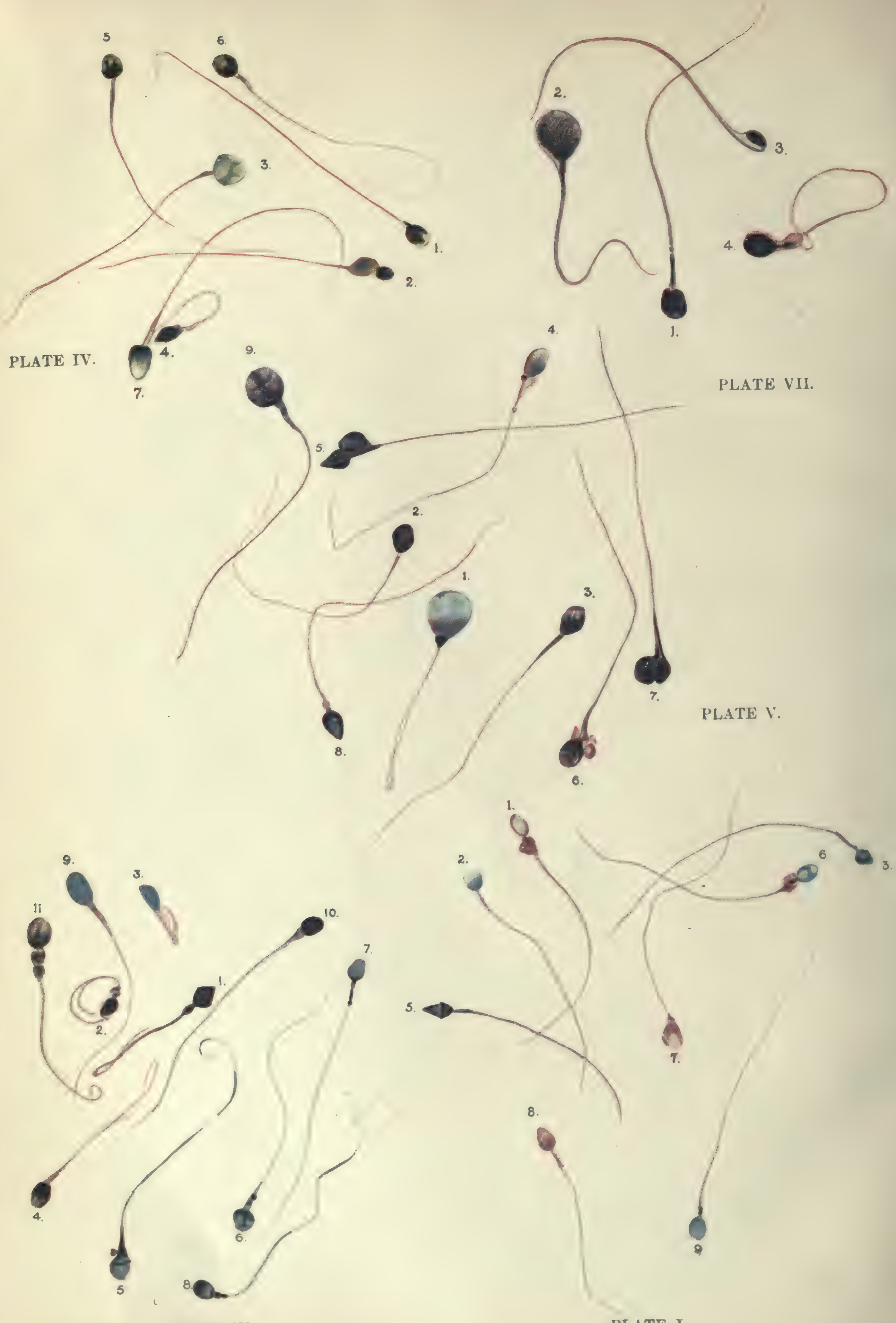

PLATE IV.

PLATE VII.

PLATE V.

PLATE IX.

PLATE I.

8 1-

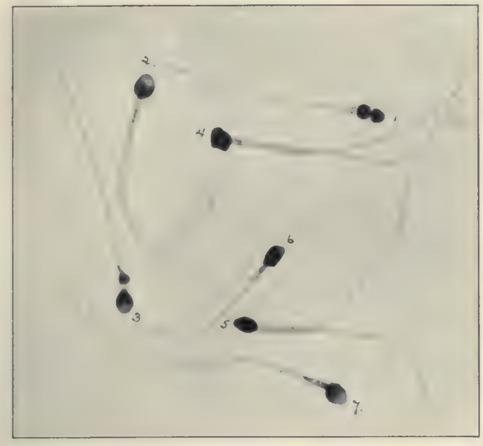

PLATE II.

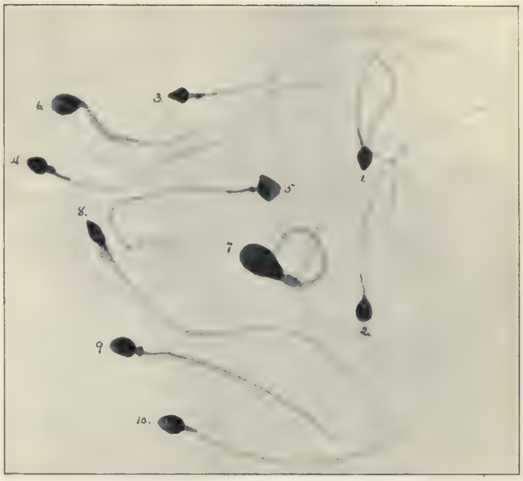

PLATE III.

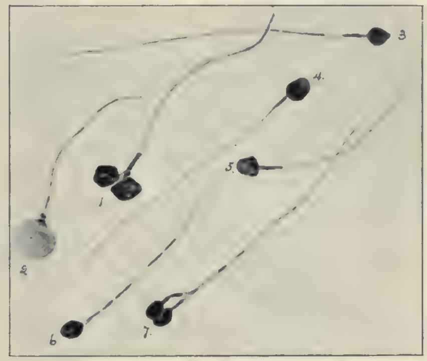

PLATE VI.

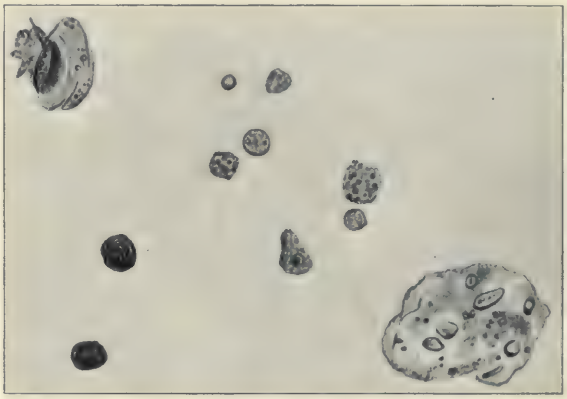

PLATE VIII.

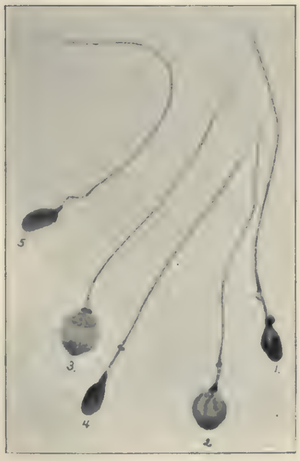

PLATE X.

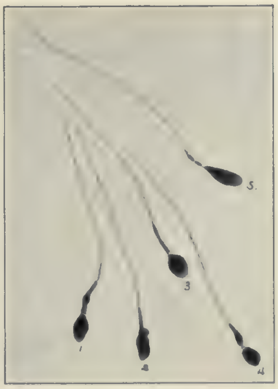

PLATE XI.

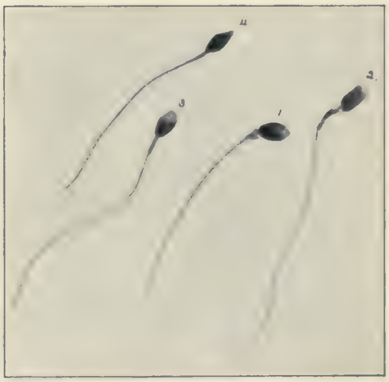

PLATE XIII.

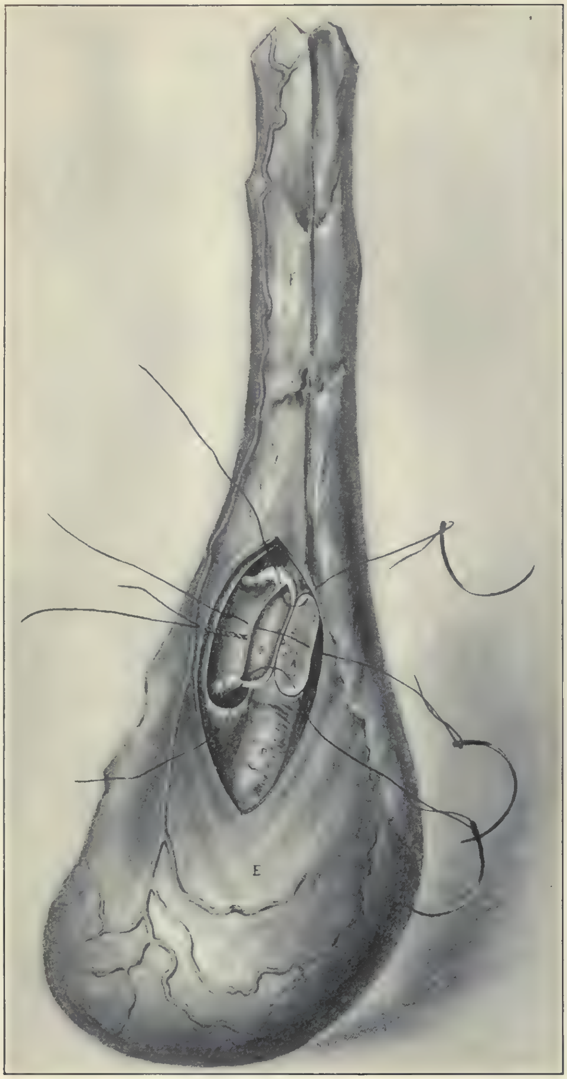

PLATE XIV.

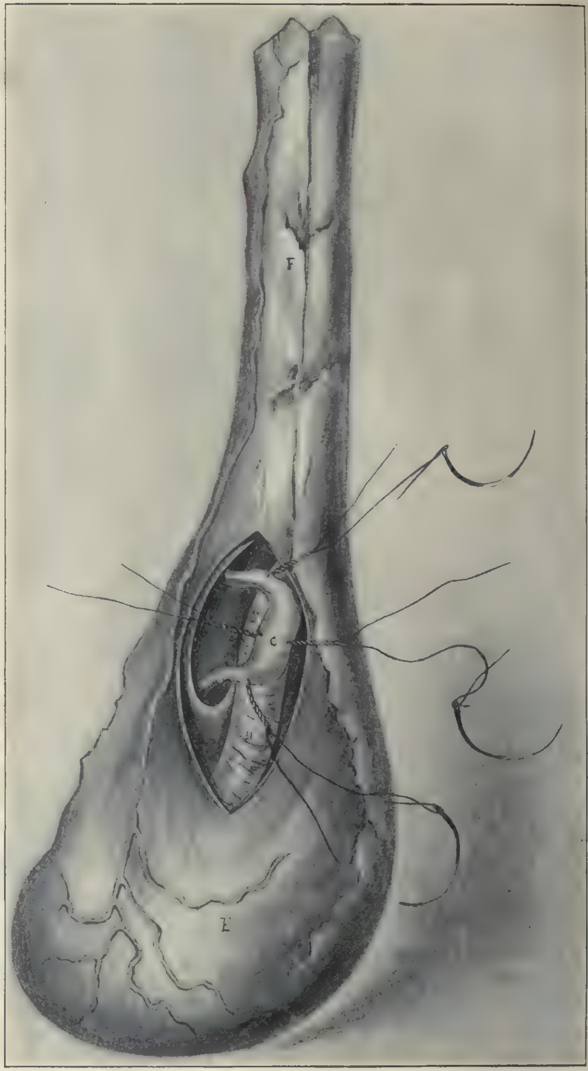

PLATE XV.

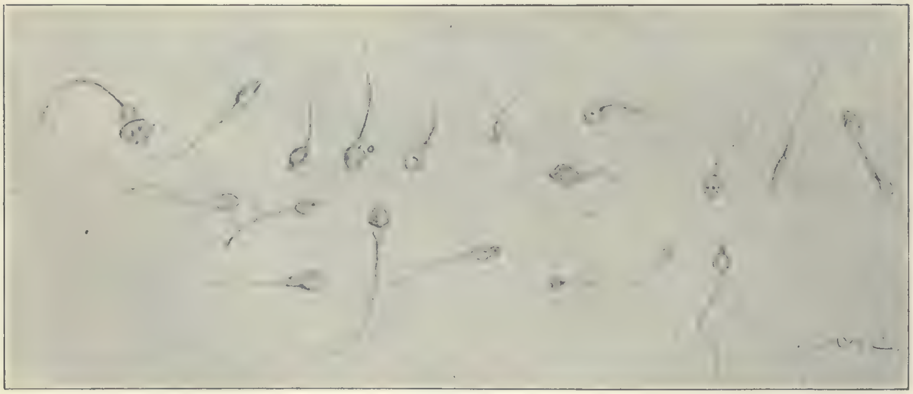

PLATE A.

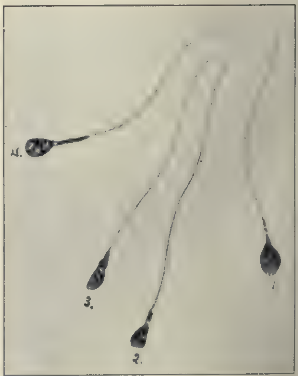

PLATE XII.

cell 1, Plate V. All the other giants stained a red violet; hence, according to Watasé, should represent undeveloped cells, but cells which contained more of the true sperm substance than those shown in 7 and 8 of Plate I. The latter, except for their red stain, would not be classed as abnormal cells. In the "Germantown" sample cells of both kinds were found; some were violet and some were blue, but none were found of the distinctly eosinophilous character.

In some cells, at least, by using three dyes a further selection in staining can be brought out. This is illustrated in Plate IV., where the forepart of the head is yellow (orange G), the chromatin of head, centrosomes, and axial filaments is black (ironhæmatoxylin), and the protoplasm of tail and middle piece is pink (eosin).

Such a selection would indicate that the chemical composition of the anterior part of the head is different from that of the protoplasm of middle piece and tail, though, as orange G is a cytoplasm stain, they have probably more or less in common. If, too, the "head cap" persists in man, as Ballowitz states that it probably does, it must consist of a modified form of protoplasm, since no red envelope could be seen on the anterior portion of the heads.

On the other hand, no trace of the orange dye could be found in the protoplasm of middle piece and tail. Cell 2, Plate I., shows a deformity in which the mass behind the black ball (the head?) is yellow in its anterior and pink in its posterior part, these colors gradually blending without any line of demarcation. This large, loosely constructed mass occupies the position of the middle piece; the head has no trace of an anterior portion as distinguished from a posterior, hence it may be that the relative positions of these chemically different substances have been confused. Whatever may be this substance, it is fairly constant, and is seen even in the giant heads, where it forms a considerable portion of the head, though it does not stain so deeply as in the smaller forms.

The question of development of the sperm cells outside of the testis has been studied by measurements and by staining to bring out differences of structure, as discussed under the heading "Study of the Sperm Cells from the Testis." What is there stated is confirmed, to a certain extent, by the study of the second "Germantown" specimen, representing as it does the sperm cells which go from the testicle into the globus major, and thence to the anastomosed vas deferens.

The most prominent feature about the cells from the body of the epididymis is the marked staining of the middle piece and the presence in it of one or two distinct enlargements. A cell having similar middle pieces was seen in the "Germantown" material. Indeed, 50 per cent. of the cells are such forms. The heads here vary much more than did the heads observed in the epididymis; but the middle pieces, even when lacking enlargements, stain more freely than usual, and spiral markings in many of them are distinctly visible, a condition, according to Ballowitz, found in testicle cells. The "Germantown" cells were freely motile, but so also are the cells from the globus major of the dog. That a difference does exist between these cells and those which pass along the entire tract seems fairly probable. How deep-seated this difference is cannot be said from the work done.

Motility would seem to be a more trustworthy proof of the fertility of spermatozoa than any afforded by microscopical study, and persistence of motility should, on general principles, form a fairly reliable index to health and vitality.

EXPERIMENTAL.

In experiments on dogs* it was generally, but not always, found that the spermatozoa from all parts of the epididymis, vas, and the vasa efferentia were actively motile, but this phenomenon was not observed in spermatozoa derived from the secreting substance of the testis. The motility was less active and less prolonged than that which characterized spermatozoa ejaculated in orgasm.

We obtained motile spermatozoa from the efferent vessels of bull testes which had been on ice for thirty-six hours, and Piersol noted motility in human semen which had been kept at 40° F. for eight days.

We have frequently noted motile spermatozoa in semen which had been standing at the room temperature for three days, and have more frequently observed that all movement ceased in twenty-four hours. This was doubtless due in part to bacterial invasion and decomposition, since the urethra is never sterile.

It is generally believed that an acid medium is immediately lethal to spermatozoa. We have, however, in cases of spermatorrhœa seen the spermatozoa living for hours in an acid urine; and Lohenstein (*Deutsche med. Wochenschrift,* December 27, 1900) has shown that the prostatic secretion may be either acid or alkaline. Of 542 tests of prostatic secretion, on 80 patients, the reaction was alkaline in about 76 per cent., neutral in about 5 per cent., and acid in 20 per cent. In only 5 of the 80 cases was the reaction constantly acid. The chemical reaction of the prostatic secretion had no apparent modifying effect on the vitality of the spermatozoa.

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* The experiments upon which the work is founded were conducted in the Pepper Laboratory, University of Pennsylvania.

In the testicular secretion of bulls, rams, dogs, and rabbits we were not able to restore motility, when this was not present, by warming or by diluting with prostatic secretion or with salt or alkaline solutions, though Walker lays some stress upon the efficacy of this procedure in his experimental work, observing that dilution with prostatic fluid was especially efficient in prolonging the life of the spermatozoa. Beigel, quoted by Gross (*Krank. des Weib. Geschlechts*, Bd. ii., p. 747), noting in one case that the ejaculated sperm was thicker and more viscid than normal, found, on microscopical examination, that the spermatozoa were motionless and closely grouped side by side. The addition of a few drops of tepid water put them in lively motion, so that he advised the injection of a small amount of lukewarm water into the vagina immediately after coitus, and the woman subsequently bore several children.

Absence of spermatozoa from the semen, an absolute sign of sterility, may be due to lesions in the testicles or to abnormality or obstruction of their efferent ducts. The common cause of azoöspermia is an obliterating double epididymitis, usually of gonorrhœal origin.

The testicle forms an exception to other secreting glands, from the fact that complete obliteration of its duct is not followed by atrophy or by any appreciable change in its function or nutrition.

There is a popular belief among physicians to the effect that gonorrhœal epididymitis, if at all severe, forever prevents the discharge of spermatozoa from the testicle of the affected side, and that if both sides are involved in this inflammation the patient will remain sterile, though there may be no alteration in his sexual appetite or ability. This belief is founded on the statement of Godard, who, in 1857, examined the semen of 30 patients who had suffered from bilateral epididymitis; spermatozoa were absent in all. Liégeois, of 83 cases, could find spermatozoa in but 8. J. William White, of 117 cases, noted restoration in but 13. Bollet, Bumstead, Jullien, and Fürbringer all state that the appearance of spermatozoa in the semen after double epididymitis is the exception, and Monod and Terrillon find that in these cases spermatozoa are not observed. Against these opinions may be quoted that of Fournier, who believes that the obliteration of the spermatic duct incident to epididymitis is temporary in the vast majority of cases; while Hardy holds that, after a period varying from two months to two years, such patients are able to procreate, sterility in reality being an exceedingly rare sequel of double epididymitis.

It is clear that the immediate effect of a severe double epididymitis is to cause disappearance of the spermatozoa from the semen; it is also evident that the disappearance may be permanent, since many cases of sterility are recorded, the patients reporting for examination months or years after the original double epididymitis. It is certain that not all of these cases remain sterile, and that a much larger percentage than statistics would show regain full power, since when this is the case the physician has no further opportunity of making an examination; while if sterility results the patient is almost certain to present himself for professional advice. The question as to the percentage of cases in which recovery is complete, and the percentage in which sterility results, can be settled only by prolonged clinical observation of a large number of cases of double epididymitis. Balzer and Souplet (*Annales de Dermatol. et de Syphilograph.*, tome iii., May, 1892), in the hope of rendering knowledge upon these points more definite, have contributed the results of examinations upon 46 cases of recent double epididymitis. Of 34 such examinations spermatozoa were found in but 3; six old cases, in which examinations were made more than six months after the last attack of epididymitis, showed spermatozoa in 5. This result apparently confirms the statement of Gosselin, who wrote that obliteration of the ducts may continue for a variable period; it may disappear in three, four, five, or eight months, allowing the spermatozoa to escape; indeed, it is not possible to set a limit as to the time after which recovery is impossible. In some of the recent cases examined by Balzer and Souplet, spermatozoa had disappeared six days after the beginning of the inflammation—a result not in accordance with the teaching of Monod and Terrillon, who state that in double epididymitis spermatozoa persist in the semen for two or three weeks from the beginning of the attack.

In accordance with the findings of Balzer and Souplet are the results of our own examinations of the semen of patients who suffered from double gonorrhœal epididymitis. Fifteen old cases examined showed spermatozoa in fourteen. All the recent cases showed absence of spermatozoa, and this was observed in two instances even though the disease was unilateral. In addition to the fifteen old cases examined, simply because they gave a history of double epididymitis, and not because of any complaint on their part, six more old cases were examined on account of supposed sterility, their wives never having conceived. All these patients were sterile, and all gave a history of bilateral epididymitis. It is interesting to note that this experience is paralleled by that of Balzer and Souplet, who examined the semen of five men referred to them by Fournier from his private practice, probably on account of suspected sterility. In the discharge of none of these patients were spermatozoa found.

The practical application of these facts is that patients should be told when suffering from an attack of double epididymitis that they will be temporarily sterile, but that the power of impregnation will probably return; that there is a possibility that sterility may be permanent, hence, should an unfruitful marriage take place, the semen should be examined before subjecting the woman to treatment at the hands of the gynecologist; and, most important of all, that treatment should be continued until microscopical examination shows that spermatozoa are again present in the semen.

Terrillon (*Bull. et Mem. de la Societe de Chirurgie*, 1881), in conjunction with Malassez, made microscopical examinations of the human epididymis which had been subject to gonorrhœal inflammation, and of the epididymis of dogs which had suffered from an inflammation excited by irritant injections into the vas. They observed that the inflammation attained its maximum intensity in the tail of the epididymis, becoming greatly moderated as the ducts were followed to their upper parts. The lumina were enlarged, the epithelium degenerated, void of cells, often completely desquamated, the duct walls either thinned or exhibiting a thickening due to small round-celled infiltrate, the intertubular connective tissue gorged with pigmented lymphatic cells. These inflammatory phenomena may be practically wanting in the globus major in mild cases of epididymitis, nor does the testicle present any lesion except congestion and possibly slight œdema.

Neither the extent of the palpable swelling in acute epididymitis nor the acuteness of the pain is a true index as to the amount of involvement of the canal of the epididymis, since the tumefaction is due to an inflammatory infiltrate into the connective tissue surrounding the vas and the epididymis; the agonizing pain to a vaginitis, which is practically always present. Though a moderate induration may persist in and about the tail of the epididymis and the convoluted portion of the vas, Terrillon believes that because of the yielding nature of the structure it rarely causes a complete obliteration. Patients who have had repeated attacks of epididymitis, and those whose attacks have been characterized by symptoms of unusual severity, do not seem more prone than others to suffer from the obliterating process.

A study of these cases seems to show that sterility is most likely to follow a bilateral epididymitis, the treatment of which, because of the comparative mildness of the symptoms, has been casual. As in the case of larger mucous channels, permanent narrowing or blocking is the result of a chronic, long-continued inflammation rather than of one which, even though hyperacute, is of short duration. Gosselin (*Archiv. Gén.*, Ser. 4 and 5) first pointed out that obliteration of the seminal passage is usually due to gonorrhœa, and that it is with few exceptions confined to the epididymis, the vasa deferentia alone being rarely involved. His observations and those of Terrillon and Malassez have been repeatedly confirmed.

It seems clear, then, that azoöspermia following a double epididymitis is almost certainly due to obstruction in the tail of the epididymis; that motile spermatozoa may be found in great numbers in the epididymis above the block; that the route is usually clear from the block to the urethra.

Should there be no immediate mechanical treatment applicable to the overcoming of the obstruction, because of the extreme minuteness and the convoluted structure of the tubes of the epididymis, the possibility of switching out the seat of obstruction by a short circuit naturally suggests itself. This short circuit can be made by attaching the vas to any part of the epididymis on the testicular side of the obstruction or to the vasa efferentia.

The epididymis is usually regarded as a duct provided with ciliated epithelium of lessening calibre toward the tail, and having for its sole function the passage of the spermatozoa from the vasa efferentia into the convolutions of the vas.

Myers (*Journal Anat. and Physiol.*, Lond., 1897, vol. xxxii., Part I.) finds that at one period in the life-history of the epididymis appearances very like budding occur. He regards the epididymis as almost certainly a secretory tube, the secretion consisting of separated portions of the lining cells and being destined for the nourishment of the sperm cells, the vas probably having the same function.

Both the microscopical study and observations upon the motility of cells derived from the efferent vessels, the epididymis, and the vas appear to corroborate this view. It is, however, probable that a passage through the entire epididymis, or even through a greater portion of it, is not necessary to the fertility of the spermatozoa.

Basing the hope of successful results on the facts that actively motile, well-formed spermatozoa are found in all parts of the epididymis, three dogs were etherized and subjected to the anastomosis operation. In all the vas was ligatured and cut obliquely above the seat of ligation, a piece was snipped out of the head or body of the epididymis, and into this opening the split vas end was implanted by means of one suture in the first case, two sutures in the other two.

From the urethra of the first dog—a half-breed pug, weighing sixteen and a half pounds, operated on December 6, 1901, well-formed, non-motile spermatozoa, blood, and epithelium were obtained as the result of an orgasm seventeen days later. Non-motile spermatozoa were twice obtained after this, but it was not until January 1, 1902, that motile spermatozoa were found in the urine after an unsuccessful attempt to obtain the seminal fluid.

A black mongrel, weighing twenty-seven and a half pounds, operated on December 16, 1901, exhibited in an emission which occurred two weeks later, and in one a week after that, many active spermatozoa.

In the semen of the third dog—a yellow mongrel, weighing twenty-four and a quarter pounds—active spermatozoa were also found.

The results of these experiments seemed conclusive enough to justify performing an anastomosing operation upon man when a childless marriage was dependent upon azoöspermia consequent upon a double obliterating epididymitis. Such a patient had presented himself two years before, and, after the futility of conservative treatment had been demonstrated, was advised to have such an anastomosing operation performed. He was told that it had not previously been done, and that there was no experimental evidence to prove that it would be successful; but that it was devoid of danger, could not make his condition worse, and offered reasonable prospect of success. He very properly refused to subject himself to such a procedure until its remedial efficacy was at least demonstrated on dogs. When told of the results obtained in the experimental study, he readily consented to the operation.

He is a healthy young man, most anxious for children, as is his wife, who had been subjected to dilatation and curettement before it was discovered that her husband was sterile. In the fall of 1897 he suffered from gleet, having had acute urethritis—one attack twelve years, and one four years before. Both attacks were severe, the first being complicated by rheumatism, the second by bilateral epididymitis. There was a large calibre structure in the bulbous urethra, with ulceration behind it, also some follicular prostatitis. Gradual dilatation, irrigation, and massage cured his gleet. In the spring of 1898 it was found that the semen contained no spermatozoa. There was no nodulation of the tails of the epididymis The right testis was the larger of the two. He was directed to wear a sweating suspensory bandage, and was ordered testicular and prostatic massage. Repeated examinations failed to show the presence of spermatozoa until March, 1901, when careful search enabled the observer to detect two or three ill-formed dead ones in each cover-glass preparation. In the fall of 1901 examinations failed to demonstrate even a single spermatozoön. The findings just before operation have been given in another part of this paper.

On December 24th, under ether, the vas of the left side was freed at about the level of the top of the testis, and, by means of a sharp-pointed pair of scissors and a slender bistoury and a grooved director, such as are used by ophthalmologists, its lumen was opened by a longitudinal cut one-quarter of an inch long. The epididymis was then approached from the outer side, and its entire length was exposed. An incision into the tail failed to show the presence of a milky fluid, though cover-glass preparations subsequently examined demonstrated a few spermatozoa in the expressed fluid. A portion of the head was then picked up in toothed forceps and excised. A few minute, yellowish drops at once appeared on the resulting cut surface, made up in the main of spermatozoa, some of which, examined fifteen minutes later, were motile. Into this wound of the epididymis the vas was implanted by means of four fine silver-wire sutures carried on small-face needles from the outer surface of the vas into its lumen, thence, from the cut surface of the opening made into the epididymis, through its fibrous tunic. A suture was placed at either end of the vas incision, and the latter was held open by the two other sutures, one to either side (see Plates I., XIV., and XV.). The skin was closed by catgut. The dressing slipped the next day, exposing the wound, which suppurated superficially.

Semen sent for examination nineteen days after operation and twelve hours after emission showed motile spermatozoa, apparently healthy, but corresponding on microscopical study to the type observed in the epididymis of the human testis removed after death and subjected to examination.

The approach to the epididymis is not difficult, nor does it seriously endanger the nutrition of the testes by interfering with its blood-supply. The vas lies behind the spermatic artery, which sends its main branches forward to the inner side of the epididymis, anastomosing freely at this point with the artery of the vas. The portion of the vas which is to be used for anastomosis is to be carefully dissected free from its surrounding vessels and nerves, and carried to the outer side of the vascular plexus of the cord until it can be applied readily to the exposed surfaces of the epididymis. Because of the smallness of the structures involved, the operation is tedious rather than difficult.

Scaduto (*Annales de Maladies des Organes Genito-Urinaire*, 1901, No. 31) practised a similar operation on dogs, anastomosing the vas with the rete testis or with some other part of the gland, hoping by this procedure to preserve function and even fertility in man after resection of the epididymis for the removal of tuberculous infiltration, holding that everyone concedes that the epididymis has no function other than that of a conductor, the entire process of spermatogenesis being completed in the testes. His results were, in the main, unsatisfactory, some dogs having escaped, others having suppurated. In a few post-mortems, however, performed in one case months after the experimental operation, gelatin injected into the vas filled the rete, thus showing the success of the procedure; nor was there about the seat of the anastomosis any sign of cicatricial contraction. Bardenheuer (quoted by Scaduto) attempted a similar anastomosis, cutting the vas across and suturing it into the rete testis. He did not succeed, nor did Scaduto demonstrate the efficacy of his experiments by finding spermatozoa in the urethra.

These two are the only references found bearing upon this operation, which was proposed before knowing of any work having been done in this direction.

As to the ultimate effect of this procedure, it might be feared that the duct of the epididymis would close by cicatricial contraction, and this might follow were its lumen not occluded. With an active testicle and complete obliteration of the tail of the epididymis, there should, reasoning by analogy, be little tendency for the duct divided above the occlusion to close. Indeed, Faterini (*Clinica Moderna*, Anno iv., Nos. 47–49) observed, after cross-section of the epididymis, the development of retention cysts on the testicular side of the cut, which ultimately formed a communication with the vessels on the vas side, thus restoring the continuity of the duct.

If it be conceded that spermatozoa taken from the vasa efferentia or the head or body of the epididymis are fertile, it is at least conceivable that, by an epididymotomy or epididymectomy performed upon a husband, and through an opening made in the abdominal walls of the wife, an ovum could be fertilized without danger of provoking a concurrent infection, and, moreover, should the wife, either from malformation or disease, be unable to carry the product of conception to full term and safe delivery, it is theoretically possible to implant this fertile ovum into the Fallopian tube or uterus of a healthy woman and have it undergo its proper physiological development. The circumstances under which such a procedure might be considered are not hard to imagine. Heape (*Proc. Roy. Soc.*, xlviii., pp. 457, 458), in a preliminary note, has proved its practicability in animals. He implanted two fertilized ova of an Angora rabbit into the Fallopian tube of a Belgian hare. The Belgian hare had six young, four being Belgian hares and two perfect Angora rabbits. In this case the impregnation was not artificial; it, however, demonstrated the possibility of making use of the uterus of one variety of rabbit as a medium for the growth and complete development of the fertilized ova of another variety.

It may be profitable to accentuate by a final summary the facts which seem to have been partly or completely demonstrated by a study of the subject:

In sterile marriages the fault certainly lies with the husband in from 10 to 15 per cent. of cases; probably in a still larger percentage.

Though absence of motile spermatozoa is a proof of sterility, their presence does not necessarily demonstrate that the semen is fertile.

Microscopical study shows that spermatozoa, though conforming to a general type, differ greatly, and even in the same individual, in conformation, size, and color reaction. In spite of these differences, it seems possible to recognize the normal and probably fertile organisms.

In their passage through the epididymis the spermatozoa undergo developmental changes so marked as to be easily recognizable; hence, it is probable that the epididymis is not a mere conduit.

The prolongation of motility is a better index of fertility than the mere fact of motility.

The commonest local cause of sterility in the male is obliterating bilateral epididymitis of urethral origin. Bilateral epididymitis is comparatively rare. Permanent obliteration of the tube of the epididymis is its exceptional rather than its usual termination, and is most effectually avoided by prolonged treatment. When the obliteration persists it is in the tail of the epididymis.

Azoöspermia resulting from obliteration in the tail of the epididymis can be easily and safely overcome by forming an anastomosis between the head or body of the epididymis and the vas. Ejaculations following this anastomosis swarm with motile spermatozoa. Whether these be fertile, and whether the vaso-epididymal anastomosis will persist, can be determined only by prolonged observation.

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